Acta Odontologica Scandinavica. 2015; 73: 433–440

informa healthcare

ORIGINAL ARTICLE

Craniofacial and pharyngeal airway morphology in patients with acromegaly

BURCU BALOS TUNCER[1], NEHIR CANIGUR BAVBEK[1], CIGDEM OZKAN[2], CUMHUR TUNCER[1], ALEV EROGLU ALTINOVA[2], KAHRAMAN GUNGOR[3], MUJDE AKTURK[2] & FUSUN BALOS TORUNER[2]

[1]*Department of Orthodontics, Faculty of Dentistry,* [2]*Department of Endocrinology and Metabolism, Faculty of Medicine, and* [3]*Department of Oral & Dentomaxillofacial Radiology, Faculty of Dentistry, Gazi University, Ankara, Turkey*

Abstract

Objective. The aim of this study was to assess differences in craniofacial characteristics, upper spine and pharyngeal airway morphology in patients with acromegaly compared with healthy individuals. ***Materials and methods.*** Twenty-one patients with acromegaly were compared with 22 controls by linear and angular measurements on cephalograms. The differences between the mean values of cephalometric parameters were analyzed with Mann-Whitney U-test. ***Results.*** With respect to controls, anterior ($p < 0.05$), middle ($p < 0.01$) and posterior ($p < 0.05$) cranial base lengths were increased, sella turcica was enlarged ($p < 0.001$) and upper spine morphology demonstrated differences in the height of atlas ($p < 0.01$) and axis ($p < 0.05$) in patients with acromegaly. Craniofacial changes were predominantly found in the frontal bone ($p < 0.01$) and the mandible ($p < 0.05$). As for the airway, patients with acromegaly exhibited diminished dimensions at nasal ($p < 0.001$), uvular ($p < 0.01$), mandibular ($p < 0.01$) pharyngeal levels and at the narrowest point of the pharyngeal airway space ($p < 0.001$) compared to healthy controls. Soft palate width was significantly higher ($p < 0.001$) and the hyoid bone was more vertically positioned ($p < 0.01$) in patients with acromegaly. ***Conclusions.*** Current results point to the importance of the reduced airway dimensions and that dentists and/or orthodontists should be aware of the cranial or dental abnormalities in patients with acromegaly.

Key Words: *acromegaly, craniofacial morphology, upper spine morphology, pharyngeal airway*

Introduction

Acromegaly is a relatively rare disorder due to overproduction of growth hormone (GH) and increased levels of insulin like growth factor-1 (IGF-1), predominantly caused by a pituitary adenoma at post-pubertal period [1]. The diagnosis of acromegaly usually takes 5–10-years depending on the slow development of clinical alterations. Acromegaly is associated with cardiovascular and respiratory diseases, diabetes mellitus, joint problems, bone and soft tissue overgrowth [2]. Changes in facial features mainly include mandibular overgrowth, soft tissue prominence at forehead, nose, lips and chin [3,4]. Excessive growth may stop after the removal of tumor, but bony changes may persist and require orthognathic surgery [5]. There are a limited number of case reports emphasizing the alterations in orofacial features [4,6,7] and orthognathic surgical approaches [3,8] in patients with acromegaly [9].

Recent knowledge has also revealed a high prevalence of obstructive sleep apnea syndrome (OSAS) in patients with acromegaly [8,10,11]. Still, data on pharyngeal airway morphology in patients with acromegaly is limited [12–14]. Dentists, in particular orthodontists, might be the first consultants to diagnose acromegaly, so they should be aware of the symptoms and management of such patients, considering respiratory tract dysfunctions. Evaluation of lateral cephalograms may be helpful to detect skull abnormalities, especially problems in the cranial and cervical vertebrae regions, as well as airway morphology [15].

Taken together, the objectives of this study were to evaluate the craniofacial morphological differences,

Correspondence: Burcu Balos Tuncer, Gazi University, Faculty of Dentistry, Department of Orthodontics, Ankara, Turkey. Tel: +903122034299. Fax: +903124687547. E-mail: burcubalostuncer@yahoo.com

(Received 17 June 2014; accepted 6 October 2014)

ISSN 0001-6357 print/ISSN 1502-3850 online © 2015 Informa Healthcare
DOI: 10.3109/00016357.2014.979868

including upper spine morphology, and to identify the pharyngeal airway morphology of patients with acromegaly and compare it with healthy controls.

Materials and methods

Twenty-one patients with acromegaly (nine male, 12 female; mean age = 47.9 ± 10.5 years) who attended Gazi University Department of Endocrinology and Metabolism were included in the study. The diagnosis of acromegaly was based on serum GH and IGF-1 levels and pituitary magnetic resonance imaging as well as clinical features. All patients were treated with trans-sphenoidal surgery. The mean body mass index (BMI) was 30.2 ± 6.0 kg/m^2. The disease duration was 5.7 ± 6.4 years. Eleven out of 21 patients were on somatostatin analog therapy. The disease was still active in nine of the patients. Intraoral examinations were performed by the same researcher (N.C.B).

The control group was composed of 22 healthy subjects (12 male, 10 female; mean age = 41.4 ± 18.3 years) who had indication for cephalometric radiographs due to various clinical reasons (prior to orthodontic treatment, planning for implant angulations and/or occlusal plane constructions, enlightening the degree of teeth which had drifted in relation to the occlusal plane or establishment of vertical jaw relation before stabilization occlusal splints) in different departments. The inclusion criteria for the control group were; Caucasian ethnicity, no chronic diseases, no craniofacial anomaly and no previous orthodontic treatment history. All control patients were fully informed that their radiographs would be used for an investigation and all participants gave written informed consent. This study was approved by the Ethics Committee of Gazi University (77082166-604.01.02-12555).

Cephalometric measurements

Lateral cephalograms were taken in a cephalostat (Orthophos XG 5 DS/Ceph; Sirona Dental System, Bensheim, Germany; C3 30 × 23, at 200–240 V, 12 mA) in maximal intercuspation with the lips in repose and the Frankfort plane horizontal to the floor, according to the natural head position, by a single technician. The distance from the focus of the radiographic device to the mid-sagittal plane of the patient was 150 cm and the distance from the film to the mid-sagittal plane was 20 cm. Since no correction was made for cephalometric measurements, all linear measurements had a 10% enlargement factor included. All cephalometrics were manually traced and evaluated by the same researcher (B.B.T). One of the researchers (C.T) covered the names of the patients and their groups with a sticker to prevent any bias before the main observer (B.B.T) performed the cephalometric tracings and measurements.

Thirty-eight linear and 18 angular measurements were performed on lateral cephalograms in order to evaluate the cranial, vertebral, maxillary, mandibular and pharyngeal airway morphology [12,16], by the same researcher (Figure 1). Basic reference planes used in this study were the sella-nasion plane (SN) and the Frankfurt horizontal plane (FH). The following parameters were measured for the evaluation of the cranial fossa: anterior cranial base length (S-N); posterior cranial base length (S-Ba); overall length of the cranial base (Ba-N); middle cranial base morphology (Ar-Se, Ar-Se-Pm); cranial base angle (N-S-Ba); and posterior cranial base morphology (d-s-iop, s-iop, d-p) and sella turcica morphology (S depth, S length). The landmarks for upper spine morphology were calculated according to a previous report [16]. The height of the anterior tubercule: atlas (Height AT), the height of the posterior arch of the atlas (D1), the length of the atlas (A-P); the height of the dens (DU-DL) and the height of the dorsal arch of the axis (D2).

Evaluation of frontal bone included calculations of supraorbital ridge protrusion measured from sella to glabella (S-G), frontal bone slope (S-N-F) and frontal sinus width (F1-F2). Maxillary protrusion was assessed by SNA and FH-NA angles, length of the maxilla was measured by Ba-ANS, Co-A and ANS-PNS dimensions. Evaluation of mandibular protrusion included SNB, FH-NPg and SN-Pg angles; mandibular dimensions were performed by corpus length (Go-Gn, Ba-Gn, Ba-B, Co-Gn), ramus length (Ar-Go) and Pg-NB measurements. Sagittal maxillomandibular relation was measured by ANB angle and angle of convexity (N-A-Pg). Vertical skeletal assessments required measurements of the maxillary inclination (SN-ANS-PNS), mandibular inclination in relation to SN and FH planes (SN-GoGn, FH-Go-Me, respectively), sella angle (N-S-Ar), articular angle (S-Ar-Go) and gonial angle (Ar-Go-Me). Also the anterior and posterior lower facial height (ANS-Me, Go-PNS, respectively), upper anterior facial height (N-ANS) and total anterior and posterior facial heights (N-Me, S-Go) were measured.

The following dimensions were calculated to evaluate the pharyngeal airway space (PAS): depth of the bony pharyngeal space (Ba-PNS), nasal PAS through nasal line passing through ANS and PNS points (NL-PAS); PAS at the tip of the uvula (UL-PAS); and the narrowest dimension of PAS (Min-PAS) and mandibular PAS (ML-PAS) through Go and Me. Also the length (PNS-UT) and the width of the soft palate (U1-U2) and the angle between the uvular axis and the nasal plane (ANS-PNS-UT) were assessed. The vertical and anterio-posterior position of the hyoid bone was measured by the perpendicular distance from the most superior point of the hyoid bone to the FH plane (H-FH) and the distance from the

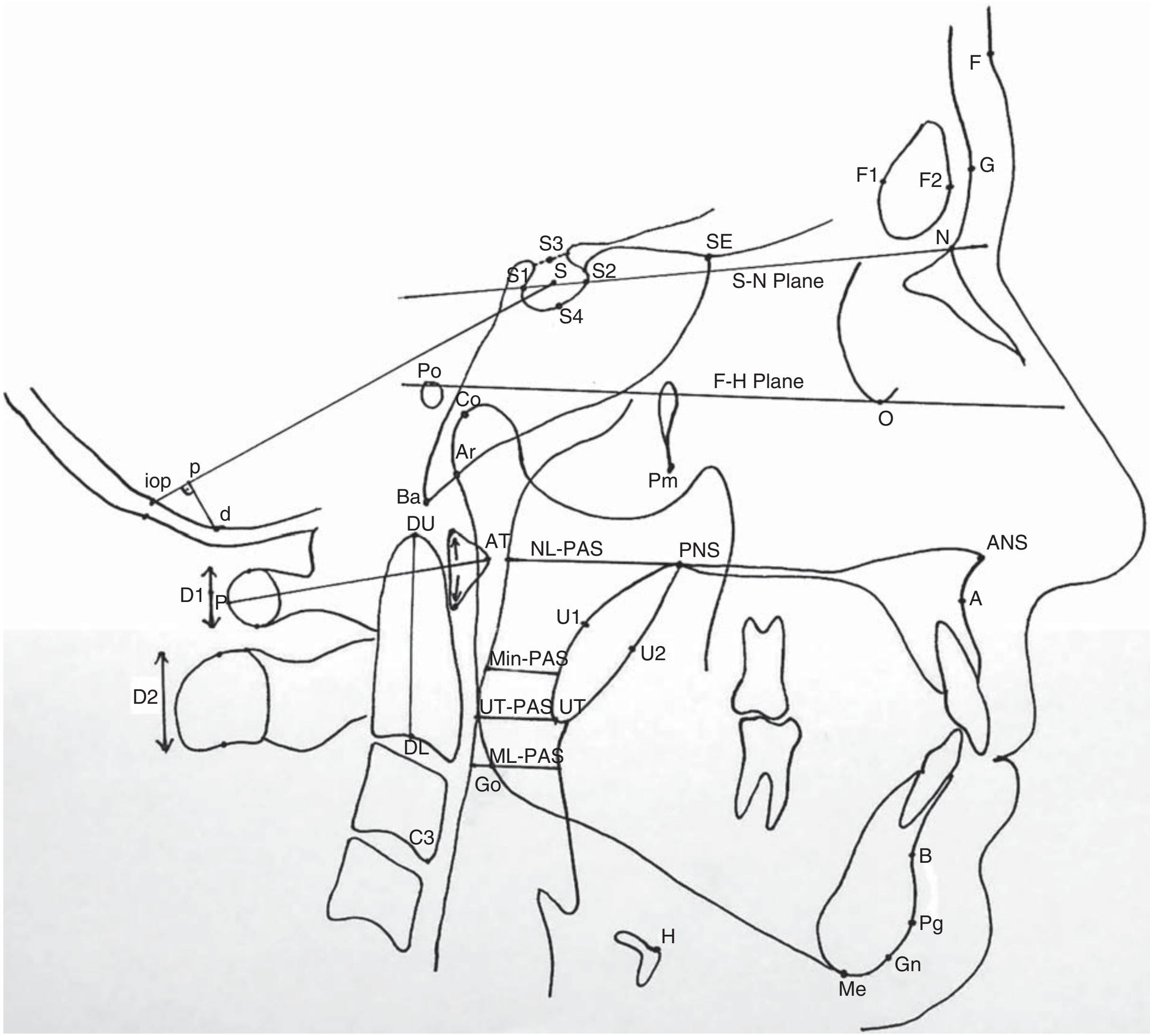

Figure 1. Definitions of cephalometric landmarks and reference planes: (1) S, midpoint of sella turcica; (2) S1, point of intersection between posterior margin of sella turcica through SN plane; (3) S2, point of intersection between anterior margin of sella turcica through SN plane; (4) S3, center of the dorsum and tuberculum sella; (5) S4, deepest point on sella turcica; (6) SE, sphenoethimoidal junction; (7) Ba, most inferior point on anterior foramen magnum; (8) d, the deepest point in posterior cranial fossa; (9) iop, internal occipital protuberance; (10) p, point constructed by the perpendicular from point d to s-iop; (11) N, anterior point at nasofrontal suture; (12) F1, point of intersection between posterior contour of frontal sinus and line connecting S-G; (13) F2, point of intersection between anterior contour of frontal sinus and line connecting S-G; (14) G, the most prominent point of the supraorbital ridge; (15) F, intersection of the perpendicular to nasion-bregma plane through its mid-point and lamina externa of the cranial vault; (16) Co, most postero-superior point on the condylar head; (17) Ar, intersection of inferior contour of the cranial base and posterior contour of ramus; (18) Pm, most inferior point of pterygomaxillary fissure; (19) O, most inferior point of the orbit; (20) Po, most superior point of external auditory meatus; (21) ANS, most anterior point of anterior nasal spine; (22) PNS, most posterior point of nasal spine; (23) A, deepest point in concavity of anterior maxilla; (24) B, deepest point in concavity of anterior mandible; (25) Pg, most anterior point of bony chin; (26) Gn; most anterior–inferior point of bony chin; (27) Me, most inferior point of bony chin; (28) Go, point constructed by bisecting the posterior and inferior borders of the mandible; (29) H, most antero-superior point of the hyoid bone; (30) UT, tip of uvula; (31) U1, posterior point of uvula at the largest diameter; (32) U2, anterior point of uvula at the largest diameter; (33) S-N plane, line through S and N; (34) FH plane, line through Po and O.

anterio-inferior point of the third cervical vertebra point to H (C3-H).

Statistical analysis

The Statistical Package for Social Sciences SPSS Version 21.0 (USA) was used for data analysis. Numerical variables were presented as mean (SD). Normality of distribution for parameters was assessed with Shapiro Wilks test. The differences between the mean values of cephalometric parameters were analyzed with Mann-Whitney U-test, when parametric test assumptions were not satisfied. The correlation between numerical variables was evaluated with Spearman correlation coefficient. A p-value < 0.05 was considered statistically significant.

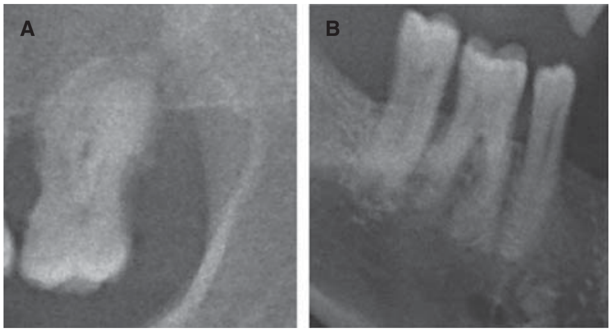

Figure 2. (A) Intra-oral radiograph related to hypercementosis in relation to upper molar and (B) hypercementosis related to mandibular posterior region.

Results

In relation to extra-oral examinations, patients with acromegaly demonstrated marked frontal bossing, widened and thickened noses, thickened lips and prominent chins. Intra-oral examinations showed enlarged tongues. Multiple tooth loss was noted in 10 patients, while three patients had no tooth loss. Panoramic radiographs revealed hypercementosis in relation to the roots of molars in 10 patients (Figures 2A and B). Panoramic and cephalometric radiographs showed remarkable deformities in nasal bone and mandible at the gonial region in two patients (Figures 3A–D). The cranial, upper spine, facial and pharyngeal airway parameters in patients with acromegaly and controls are given in Table I.

Differences in cranial fossa morphology between two groups

Anterior cranial base length (S-N, $p < 0.05$), posterior cranial base length (S-Ba, $p < 0.05$), total cranial base length (Ba-N, $p < 0.05$) and middle cranial base length (Ar-SE, $p < 0.01$) increased significantly in patients with acromegaly compared to controls. Middle cranial base inclination (Ar-SE-Pm, $p < 0.01$) was lower than controls. The length of the posterior cranial fossa (s-iop, $p < 0.05$), the height of the posterior cranial fossa (d-p, $p < 0.05$) and the depth of the posterior cranial base (d-s-iop, $p < 0.01$) were decreased in patients with acromegaly compared to control subjects. Sella turcica was significantly enlarged both in anteroposterior and vertical dimensions ($p < 0.001$).

Differences in upper spine morphology between two groups

Evaluation related to upper spine morphology showed that the height of atlas (height AT, $p < 0.01$), the height of the posterior arch of atlas (D1, $p < 0.05$) and the height of the dorsal arch of axis (D2, $p < 0.05$) were significantly larger in patients with acromegaly.

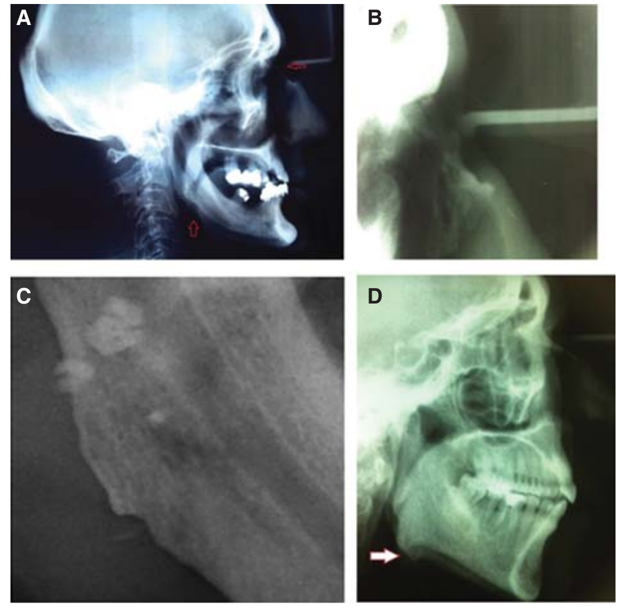

Figure 3. (A) Lateral cephalogram showing enlarged sella turcica and bony deformations, (B) bony defects at the nasal bone and (C) bone deformations at the gonial region.

Differences in facial structures between two groups

Supraorbital ridge (S-G, $p < 0.01$) was protruded, frontal bone slope (S-N-F, $p < 0.01$) was lower and frontal sinus (F1-F2, $p < 0.001$) was enlarged in patients with acromegaly. The increased maxillary bony dimension (ANS-PNS, $p < 0.001$) was the only significant difference between the groups related to maxillary morphology. Increase of mandibular corpus length (Ba-Gn, $p < 0.01$, Ba-B, $p < 0.05$, Go-Gn, $p < 0.05$) and the effective dimension of the mandible (Co-Gn, $p < 0.01$) were recorded in patients with acromegaly. The lower anterior facial height (ANS-Me, $p < 0.05$), total anterior facial height (N-Me, $p < 0.05$) and gonial angle (Ar-Go-Me, $p < 0.05$) were also significantly increased in patients with acromegaly.

Differences in pharyngeal airway morphology between two groups

Pharyngeal airway morphology was significantly reduced at nasal (NL-PAS, $p < 0.001$), uvular (UT-PAS, $p < 0.01$) and mandibular (ML-PAS, $p < 0.01$) levels and at the narrowest point of the pharyngeal airway space (Min-PAS, $p < 0.001$) in patients with acromegaly. Soft palate width was significantly higher ($p < 0.001$) and hyoid bone in patients with acromegaly was more vertically positioned ($p < 0.01$).

Correlation analysis in patients with acromegaly

Correlation between cranial morphology, upper spine morphology and airway. S-N, S-Ba and s-iop were

Table I. Cephalometric variables and comparison between two groups.

	Acromegaly group		Control group		
Variables	Mean	SD	Mean	SD	*p*
Cranial fossa morphology					
S-N (mm)	77.14	4.09	75.00	3.35	0.041
S-Ba (mm)	50.80	5.95	48.13	6.62	0.049
Ba-N (mm)	115.90	8.34	111.77	4.45	0.042
Ar-SE (mm)	64.66	6.19	59.31	4.23	0.001
Ar-SEPm (°)	32.85	5.14	36.63	4.38	0.003
N-S-Ba (°)	129.57	6.28	131.72	4.10	0.096
s-iop (mm)	84.66	4.19	87.00	6.43	0.049
d-p (mm)	7.14	3.29	9.27	2.99	0.026
d-s-iop (°)	5.38	2.47	7.04	2.14	0.009
Sella depth, S3-S4 (mm)	11.57	3.35	7.18	1.33	0.000
Sella length, S1-S2 (mm)	17.42	7.63	10.27	1.35	0.000
Upper spine morphology					
Height of atlas, height AT (mm)	15.66	2.24	13.50	2.15	0.003
Height of dorsal arch, D1 (mm)	10.61	2.33	9.04	1.58	0.025
Length of atlas, AT-P (mm)	53.23	5.00	50.95	4.45	0.209
Height of the dens, DU-DL (mm)	39.76	4.13	39.22	2.81	0.797
Height of dorsal arch of axis, D2 (mm)	15.52	2.44	13.68	2.57	0.045
Facial, Maxillary, Mandibular morphology					
S-Glabella, S-G (mm)	85.00	5.45	80.27	3.94	0.003
S-N-F (°)	90.23	4.73	95.90	6.70	0.001
F1-F2 (mm)	16.71	4.38	10.04	2.88	0.000
SNA (°)	80.71	3.84	81.00	3.74	0.770
FH-NA (°)	86.76	3.72	87.95	4.42	0.317
Ba-ANS (mm)	106.66	7.97	102.68	5.13	0.119
Co-A (mm)	96.61	6.32	94.59	4.99	0.393
ANS-PNS (mm)	60.04	4.35	54.77	3.23	0.000
SNB (°)	79.42	4.43	77.29	3.85	0.137
FH-N-Pg (°)	86.76	5.18	86.11	4.59	0.679
S-N-Pg (°)	80.69	4.3	78.50	4.35	0.141
Ba-Gn (mm)	129	9.04	121.18	8.01	0.007
Ba-B (mm)	114.47	8.54	108.50	6.32	0.015
Go-Gn (mm)	86.28	7.27	82.00	5.19	0.034
Ar-Go (mm)	58.04	6.71	55.22	6.19	0.177
Co-Gn (mm)	134.04	8.89	125.13	7.21	0.001
Pg-NB (mm)	3.23	2.66	2.45	2.19	0.286
Maxillomandibular morphology					
ANB (°)	1.28	4.44	3.7	2.2	0.062
N-A-Pg (°)	8.02	5.36	5.97	4.22	0.312
Vertical facial morphology					
SN-ANS-PNS (°)	9.14	3.30	10.00	3.51	0.238
SN-Go-Gn (°)	34.61	5.58	33.22	7.09	0.342
FH-Go-Me (°)	30.90	6.41	28.02	7.38	0.201

Table I. (*Continued*).

	Acromegaly group		Control group		
Variables	Mean	SD	Mean	SD	p
N-ANS (mm)	60.47	5.50	58.81	3.99	0.335
ANS-Me (mm)	83.33	8.23	76.59	8.34	0.016
N-Me (mm)	143.76	11.71	135.86	10.15	0.033
S-Go (mm)	92.71	9.25	88.54	7.60	0.162
Go-PNS (mm)	51.71	7.75	52.45	5.60	0.618
N-S-Ar (°)	125.80	7.06	128.40	4.82	0.119
S-Ar-Go (°)	142.57	7.83	142.18	5.43	0.922
Ar-Go-Me (°)	128.47	5.55	124.34	5.73	0.037
Pharyngeal airway morphology					
Ba-PNS (mm)	46.61	5.02	47.81	3.83	0.334
NL-PAS (mm)	24.42	4.39	31.36	3.38	0.000
UT-PAS (mm)	9.76	3.37	12.63	2.73	0.005
ML-PAS (mm)	10.28	3.55	13.45	3.43	0.006
Min-PAS (mm)	7.28	2.83	10.68	2.25	0.000
Uvula length (mm)	40.23	3.68	39.40	4.67	0.518
Uvula width, U1-U2 (mm)	11.95	1.62	8.68	1.42	0.000
ANS-PNS-UT (°)	127.66	9.11	128.27	6.16	0.922
Hyoid bone-FH (mm)	108.04	11.00	95.40	9.77	0.001
Hyoid bone-C3 (mm)	44.47	7.76	39.63	7.41	0.064

SD, Standard deviation, * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; NS, non-significant.

positively correlated with H-FH ($r = 0.592$, $p < 0.01$; $r = 0.600$, $p < 0.01$; $r = 0.434$, $p < 0.05$, respectively). There were no significant correlations between upper spine parameters with airway ($p > 0.05$).

Correlation between mandibular morphology and airway. Ba-Gn was positively correlated with UT-PAS ($r = 0.612$, $p < 0.01$), ML-PAS ($r = 0.481$, $p < 0.05$) and Min-PAS ($r = 0.514$, $p < 0.05$). Also, Ba-Gn and H-FH, H-C3 were positively correlated with each other ($r = 0.504$, $p < 0.05$; $r = 0.575$, $p < 0.01$, respectively). Go-Gn showed a positive correlation with UT-PAS ($r = 0.480$, $p < 0.05$) and ML-PAS ($r = 0.437$, $p < 0.05$). Ramus height was positively correlated with vertical and anteroposterior position of the hyoid bone ($r = 0.590$, $p < 0.01$, $r = 0.550$, $p < 0.05$, respectively).

Correlation between maxillary and vertical morphology and airway. There were no significant correlations between maxillary and vertical variables with airway ($p > 0.05$).

Correlation between disease duration, BMI and airway.. No significant correlations were found between disease duration, BMI and airway morphology ($p > 0.05$).

Correlation between disease duration and cranial morphology. Sella depth and sella length were positively correlated with disease duration revealed by coefficients $r = 0.447$, $r = 0.490$, $p < 0.05$, respectively.

Correlation between cranial morphology and upper spine morphology. The length of the atlas correlated positively with the anterior and posterior cranial base lengths ($r = 0.439$, $p < 0.05$; $r = 0.692$, $p < 0.01$, respectively) and mandibular length ($r = 0.505$, $p < 0.05$).

Correlation between disease duration, BMI and maxillary-mandibular morphology. There were no significant correlations between disease duration and BMI, maxillary and mandibular morphology ($p > 0.05$).

Discussion

There are several reports [6,12–14] describing typical craniofacial changes of patients with acromegaly, but, as far as we know, this is the first study to evaluate anterior, middle and posterior cranial fossa morphology, upper spine morphology and pharyngeal airway of patients with acromegaly in detail. In accordance with previous studies, we found greater dimensions in anterior and middle cranial bases, abnormally sized sella turcica and increased width of the frontal sinus [6,7]. It is well known that patients with acromegaly have an enlarged sella turcica, which is usually due to a pituitary adenoma [15]. Current results also revealed a positive correlation between disease duration and sella size. Expansion of frontal lobe causes deposition of frontal bone, leading to more protruded supraorbital ridge and marked frontal bossing in patients with acromegaly, as found in this study. These findings may provide further information to orthodontists to question the probability of acromegaly when evaluating lateral cephalograms.

Neurocranial bones are also affected from the disease. The cranial base is formed by endochondral ossification as well as anterior, middle and posterior cranial fossa. Cranial base growth is due to expansion of brain lobes, growth at synchondroses, ossification at sutures and cortical re-modeling [17]. Cortical re-modeling deepens the posterior cranial fossa by relocating the foramen magnum downwards [17]. Based on our results, the length, height and depth of the posterior cranial fossa were decreased in patients with acromegaly, which might be related to the differences in bone re-modeling. Articular endochondral overgrowth and subsequent ossification occur at specific sites by bony apposition-re-modeling resorption mechanism, which may involve the skull, extremities and spine [18]. Current results revealed increased dimensions of the atlas and the posterior arch of the axis in patients with acromegaly compared with controls, which might also depend on the disturbances in bone metabolism. A previous study declared that bone deformation in patients with acromegaly affects the spine, with upper dorsal kyphosis and lumbar hyperlordosis [19]. It may be considered that skeletal changes are not only due to excess growth of bone and cartilage, but also related to bone deformation [7]. Previously, correlations between upper spine morphology and posterior cranial fossa morphology had been reported, supporting the idea of a common embryological origin [16,20]. Similarly, the current results revealed a correlation between the length of atlas and anterior and posterior cranial base lengths. Recently, Gjørup et al. [16] found a positive correlation between the length of the atlas and the mandibular prognathism. Hugger et al. [21] also demonstrated an interaction between the height of the posterior arch of atlas and the forward growth of the mandible. In accordance with these studies the length of atlas showed a correlation with mandibular length in our study.

Our findings showed that craniofacial changes were predominant in the mandibular dimensions. The corpus dimension and effective mandibular length were increased in patients with acromegaly. These findings were similar to previous results and may depend on the excess GH and IGF-I stimulating periosteal bone formation, especially at the mandible [22]. Mandibular ramus length revealed no significant difference between groups, in opposition to other studies [6,12,23]. These different findings show that bony changes show great variability and are heterogeneous. The gonial angle may also increase and the shape of the mandible at the gonial region may be prominently altered in some patients, as demonstrated in our study. Again few patients demonstrated bony defects in nasal bone region. Therefore, orthodontists should be aware of similar defects and evaluate such patients in detail (Figure 3).

It is generally believed that Class III malocclusions characterized by mandibular prognathism [24] are the most common oral manifestations of acromegaly, due to re-activation of the subcondylar growth zones [25]. However, in relation to the present results there was no significant difference in ANB angle between patients with acromegaly and healthy controls as expected, thus five patients with acromegaly had skeletal Class 2, seven patient had skeletal Class 3 and nine patient had skeletal Class 1 malocclusion. This was in contrast to results of Karakıs et al. [6], but similar to a previous study [12].

In contrast to Dostalova et al. [12], who found retroposition of maxilla in patients with acromegaly, we found no significant difference in the position of maxilla, which was inconsistent with other studies [22,26]. The only significant result in our study related to maxillary morphology was the increase in maxillary bony dimension. These discrepancies declare that signs and symptoms may vary in patients with acromegaly.

Studies have indicated that patients with acromegaly are also at increased risk for developing sleep disorders such as OSAS [14,27]. Cephalometric examinations of the pharyngeal morphology can only provide two-dimensional interpretations, however close correlation between cephalometric parameters and the three-dimensional measurements from tomograms has been emphasized [14]. Current findings related that airway dimensions were significantly reduced at nasal, uvular, mandibular levels and at the narrowest point of the pharyngeal airway space in patients with acromegaly, when compared to healthy controls. We found that mandibular length and corpus dimensions were positively correlated with airway morphology. Soft tissue hypertrophy may be considered in pharyngeal obstruction, but we could not find a significant difference in soft palate dimension or inclination between two groups. Narrowing of the airway in patients with acromegaly cannot be explained only by soft palate hyperplasia. Macroglossia, obesity, pharyngeal mucosa hypertrophy and/or vertical growth pattern of the mandible should also be considered [14]. However, our findings declared no significant correlation between vertical parameters, BMI and airway morphology. This may represent that non-obese patients with acromegaly can also express reduction in airway morphology. Our data suggested that the width of the soft palate was prominently greater in patients with acromegaly than in controls, which might have an influence on the reduced airway dimensions together with the presence of macroglossia. The position of the hyoid, which plays a major role in the etiology of OSAS, was different between groups, showing a more vertical position in acromegaly patients. Correlation analysis revealed that the vertical position of the hyoid was correlated with the anterior and posterior cranial base lengths, ramus height and mandibular corpus length. Hochban et al. [14] found that patients with acromegaly having OSAS had more vertical growth pattern and a posteriorly displaced hyoid, than in acromegaly patients without OSAS. As the hyoid bone moves posteriorly, there is a tendency for the tongue to encroach upon the pharyngeal airway and, in order not to compromise the vital airway passage, the posteriorly displaced hyoid structures are guided to an inferior position [28]. Due to our findings and the high prevalence of sleep disturbances [8,14,27], evaluation of airway adequacy by cephalograms should be performed with the assistance of polysomnographic evaluations in patients with acromegaly. Orthodontists and maxillofacial surgeons should pay attention to airway morphology, especially when planning a potential orthognathic surgery.

Hypercementosis, which is an idiopathic condition characterized by the excessive build-up of cement on the roots of teeth, that can be caused by occlusal trauma, acromegaly, gigantism or the result of functional demands on teeth, was prominent in relation to posterior teeth in half of the patients with acromegaly in our study [7]. This sign can also attract dentists' attention while examining panoramic/periapical radiographs.

In conclusion, cephalometric evaluations provide beneficial knowledge for assessment of craniofacial abnormalities in patients with acromegaly. Dentists and/or orthodontists should be aware of the dental and craniofacial signs, including bony deformities related to this disease. In a clinical perspective, orthodontists should consider the reduced airway dimensions and further evaluation should be advised in patients with acromegaly.

***Declaration of interest*:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

[1] Lugo G, Pena L, Cordido F. Clinical manifestations and diagnosis of acromegaly. Int J Endocrinol 2012;2012:540398.
[2] Melmed S. Acromegaly. N Engl J Med 1990;322:966–77.
[3] Yagi T, Kawakami M, Takada K. Surgical orthodontic correction of acromegaly with mandibular prognathism. Angle Orthod 2004;74:125–31.
[4] Kaur M, Shailaja S, Mamatha SCB. Acromegaly-a case report with dentist's perspectives and review of literature. J Adv Oral Res 2012;3:17–21.
[5] Proffit WR, Fields HW Jr, Sarver DM, editors. Early stages of development. In: Contemporary Orthodontics. St.Louis, Missouri: Mosby Elsevier: 2007. p. 134-137.
[6] Karakıs D, Aktaş Yılmaz B, Dogan A, Yetkin I, Bek B. The bite force and craniofacial morphology in patients with acromegaly: a pilot study. Med Oral Patol Oral Cir Bucal 2014;19: e1–7.
[7] Kashyap RR, Babu GS, Shetty SR. Dental patient withacromegaly: a case report. J Oral Sci 2011;53:133–6; Review.
[8] Nakano H, Mishima K, Matsushita A, Suga H, Miyawaki Y, Mano T, et al. Orthognathic surgery in an acromegalic patient with obstructive sleep apnea syndrome. Sleep Breath 2013;17: 29–32.
[9] Vitral RW, Tanaka OM, Fraga MR, Rosa EA. Acromegaly in an orthodontic patient. Am J Orthod Dentofacial Orthop 2006;130:388–90.
[10] Davi MV, Carbonare LD, Giustina A, Ferrari M, Frigo A, Cascio VL. Sleep apnea syndrome is highly prevalent in acromegaly and only partially reversible after biochemical control of the disease. Eur J Endocrinol 2008;159:533–40.
[11] Chevallier M, Pontier S, Sedkaoui K, Caron P, Didier A. Characteristics of sleep apnea syndrome in a cohort of patients with acromegaly. Rev Mal Respir 2012;29:673–9.
[12] Dostálová S, Sonka K, Smahel Z, Weiss V, Marek J. Cephalometric assessment of cranial abnormalities in patients with acromegaly. J Craniomaxillofac Surg 2003;31:80–7.
[13] Dostálová S, Sonka K, Smahel Z, Weiss V, Marek J, Horinek D. Craniofacial abnormalities and their relevance for sleep apnoea syndrome aetiopathogenesis in acromegaly. Eur J Endocrinol 2001;144:491–7.
[14] Hochban W, Ehlenz K, Conradt R, Brandenburg U. Obstructive sleep apnea in acromegaly: the role of craniofacial changes. Eur Respir J 1999;14:196–202.
[15] Chang HP, Tseng YC, Chou TM. An enlarged sella turcica on cephalometric radiograph. Dentomaxillofac Radiol 2005; 34:308–12.
[16] Gjørup H, Sonnesen L, Beck-Nielsen SS, Haubek D. Upper spine morphology in hypophosphatemic rickets and healthy controls: a radiographic study. Eur J Orthod 2014; 36:217–25.
[17] Premkumar S. Textbook of craniofacial growth. 1st ed. New Delhi; Jaypee Brothers Medical Publishers; 2011.
[18] Woo CC. Radiological features and diagnosis of acromegaly. J Manipulative Physiol Ther 1988;11:206–13.
[19] Chanson P, Salenave S. Acromegaly. Orphanet J Rare Dis 2008;3:1–17.
[20] Huggare J. Association between morphology of the first cervical vertebra, head posture, and craniofacial structures. Eur J Orthod 1991;13:435–40.
[21] Huggare J. The first cervical vertebra as an indicator of mandibular growth. Eur J Orthod 1989;11:10–16.
[22] Künzler A, Farmand M. Typical changes in the viscerocranium in acromegaly. J Craniomaxillofac Surg 1991;19: 332–40.
[23] Takakura M, Kuroda T. Morphologic analysis of dentofacial structure in patients with acromegaly. Int J Adult Orthodon Ortognath Surg 1998;13:277–88.
[24] Tuncer C, Uner O. Effects of a magnetic appliance in functional Class III patients. Angle Orthod 2005;75:768–77.
[25] Tornes K, Gilhuus-Moe O. Correction of jaw deformities subsequent to treatment of acromegaly. Int J Oral Maxillofac Surg 1986;15:446–50.
[26] Pelttari L, Polo O, Rauhala E, Vuoriluoto J, Aitasalo K, Hyyppä MT, et al. Nocturnal breathing abnormalities in acromegaly after adenomectomy. Clin Endocrinol (Oxf) 1995;43:175–82.
[27] Grunstein RR, Ho KY, Sullivan CE. Sleep apnea in acromegaly. Ann Intern Med 1991;115:527–32.
[28] Graber LW. Hyoid changes following orthopedic treatment of mandibular prognathism. Angle Orthod 1978;48:33–8.