Craniofacial changes in patients with acromegaly from a surgical perspective

FLORIAN H. EBNER, M.D.,1 VERENA KÜRSCHNER, M.D.,1 KLAUS DIETZ, PH.D.,2 EVA BÜLTMANN, M.D.,4 THOMAS NÄGELE, M.D., D.Sc.,3 AND JUERGEN HONEGGER, M.D., D.Sc.1

Departments of 1Neurosurgery, 2Medical Biometry, and 3Neuroradiology, Eberhard-Karls University, Tübingen; and 4Department of Neuroradiology, Medical School, Hannover, Germany

Object. The objective of this study was to evaluate and analyze morphometric and volumetric changes of the skull due to acromegaly in areas relevant for neurosurgical practice, focusing on the surgical implications.

Methods. On preoperatively acquired CT scans, cephalometric and volumetric measurements were performed on 45 patients with acromegaly (Group A) and 45 control patients (Group B). The authors determined thickness of the cranial vault, inner and outer diameters of the skull, and the diameter of sphenoidal and maxillary sinus, as well as frontal and maxillary sinus volumetry. The morphometric and volumetric CT data of the patients with acromegaly were compared with the data of a control group and correlated with clinical parameters.

Results. Cranial vault thickness differed significantly (p < 0.0001) between the 2 groups. A correlation of the vault thickness with preoperative human growth hormone, insulin-like growth factor–I levels, and duration of clinical history in acromegaly could not be established. The outer anterior-posterior skull diameter of Group A (18.47 ± 0.94 cm) differed significantly (p = 0.0146) from Group B (17.98 ± 0.93 cm) and correlated significantly with preoperative human growth hormone (r = 0.3277; p = 0.0299) and insulin-like growth factor–I serum levels (r = 0.3756; p = 0.0120). Measurements of the anterior-posterior diameter of the sphenoidal sinus differed significantly (p = 0.0074) between patients with acromegaly and controls. Volumetric analysis of the frontal sinus resulted in a statistically significant difference (p = 0.0382) between patients with acromegaly (14.89 ± 10.85 cm³) and controls (10.06 ± 6.93 cm³).

Conclusions. Significant craniofacial changes and volumetric remodelling of the paranasal sinus occur in acromegaly. The bone alterations are of surgical importance for using the transsphenoidal approach. Detailed preoperative diagnostic examination and planning as well as selection of appropriate instruments are mandatory for safe and successful pituitary adenoma removal in patients with acromegaly. (DOI: 10.3171/2010.7.FOCUS10152)

Key Words • acromegaly • paranasal sinus • volumetry • craniofacial change • growth hormone • insulin-like growth factor
sex- and age-adjusted IGF-I levels and pathological GH secretion during an oral glucose tolerance test. A control group (Group B) consisted of 45 patients who were examined with CT scans (Sensation 16, Siemens AG) for a reason other than a disease of the pituitary gland. The controls were age-matched with the patients. Computed tomography scans were acquired preoperatively in all patients. A helical data set was available for 32 in each group.

Data Analysis

Forty-five metric measurements on transversally oriented, orbitomeatally inclined slides were performed with SIENET Sky-VA50B (Siemens AG). Volumetric analysis of 32 frontal and maxillary sinuses was performed using the BrainLAB Workstation (BrainLAB AG). The distances assessed on transversal bone window reconstructions at the Siemens workstation and volumetric assessments are reported in Table 1 and illustrated in Figs. 1 and 2.

The morphometric and volumetric CT data of the patients with acromegaly were compared with the data of the control group. Anamnestic data, preoperative human GH and IGF-I values, and secondary diagnoses were determined. The preoperative endocrinological data were assessed immediately preoperatively or prior to medical treatment in those patients who underwent short-term preoperative pretreatment. All patients underwent operations using the transsphenoidal route and histopathological examination confirmed the diagnosis of human GH-producing adenoma.

Statistical Methods

Statistical analysis was performed with JMP statistical discovery software (version 7.0.2, SAS). The mean values of continuous variables in the 2 groups were compared with the 2-sample t-test if the variances did not differ significantly (p < 0.05). We used the Welch test for significantly different variances. Normally distributed data are summarized by their means and SDs. For variables that were not normally distributed we provide medians and ranges. We calculated the Pearson correlation coefficients for the assessment of associations between continuous variables. In the case of human GH, IGF-I, and duration of clinical history, the values were log-transformed to obtain bivariate normal distribution.

Results

Twenty-four patients with acromegaly were female and 21 were male. The control group consisted of 20 females and 25 males. The median age of the 45 patients with acromegaly was 49 years (range 9–80 years), and 52 years (range 8–82 years) in the control group.

Cranial Vault

In the patients with acromegaly (Group A), the mean thickness of the frontal cranial vault was 1.12 ± 0.43 cm. In the control group (Group B), the mean thickness was 0.67 ± 0.27 cm (Fig. 3). The difference between groups was highly significant (p < 0.0001; Fig. 4). In patients with acromegaly, the mean thickness of the occipital cranial vault was 0.75 ± 0.28 cm, whereas in the control group the
Skull alterations in acromegaly

mean thickness was 0.55 ± 0.14 cm (p < 0.0001). While
the outer anterior-posterior skull diameter of Group A
(18.47 ± 0.94 cm) differed significantly (p = 0.0146) from
Group B (17.98 ± 0.93 cm), no statistical difference could
be demonstrated regarding the inner anterior-posterior
diameter of the skull (15.80 ± 0.82 cm [Group A] vs 15.97
± 0.95 cm [Group B]; p = 0.3759).

There was a statistically significant difference (p =
0.0411) between the outer lateral-lateral (right side to left
side) diameter in patients with acromegaly (14.49 ± 0.66
cm) compared with controls (14.20 ± 0.66 cm). However,
this difference was not as great as the difference in the
outer anterior-posterior skull diameter. There was no dif-
ference (p = 0.6057) in the inner lateral-lateral diameter
between Group A (13.52 ± 0.83 cm) and Group B (13.43
± 0.66 cm).

A correlation of the vault thickness with preopera-
tive GH, IGF-I levels, and duration of clinical history in
acromegaly could be established neither at the frontal
bone (r = 0.039, p = 0.8021; r = 0.1362, p = 0.3780; and
r = −0.047, p = 0.7934, respectively) nor at the occipital
bone (r = 0.2806, p = 0.0650; r = 0.2413, p = 0.1145; and
r = 0.019, p = 0.9133, respectively). The anterior-posterior
length of the skull in patients with acromegaly correlated
significantly with preoperative human GH (r = 0.3277, p
= 0.0299) and IGF-I serum levels (r = 0.3756, p = 0.0120)
as well as with duration of clinical history (r = 0.2939, p =
0.500). A correlation of these parameters with the lateral-
lateral diameter could not be established (human GH r =
−0.1590, p = 0.3082; IGF-I r = −0.1361, p = 0.3839; and
duration of clinical history r = −0.1705, p = 0.2683).

Sinus Diameter

The sinuses showed a marked difference in longitu-
dinal expansion. Measurements of the anterior-posterior
diameter of the sphenoidal sinus differed significantly (p
= 0.0074) between patients with acromegaly (3.31 ± 0.62
cm) and controls (2.92 ± 0.71 cm). Human GH (r = 0.240,
p = 0.1251) and IGF-I (r = 0.093, p = 0.5569) at presenta-
tion were not correlated with the anterior-posterior sinus
diameter. Similarly, the anterior-posterior diameter of the
maxillary sinus was significantly longer (p = 0.0042) in the acromegaly group (4.22 ± 0.30 cm) than in the control group (4.06 ± 0.24 cm). Preoperative human GH values (r = 0.115, p = 0.4590) and duration of clinical history (r = 0.212, p = 0.1624) did not correlate with maxillary sinus length.

The width of the evaluated sinuses did not differ significantly between patients with acromegaly and controls. The lateral-lateral diameter of the sphenoidal sinus was 3.53 ± 1.03 cm in Group A and 3.30 ± 0.63 cm in Group B (p = 0.2199). The lateral-lateral diameter of the maxillary sinus was 2.33 ± 0.27 cm in Group A and 2.40 ± 0.24 cm in Group B (p = 0.1766).

**Sinus Volumetry**

Volumetric analysis of the maxillary sinus resulted in a measurement of 19.47 ± 7.02 cm³ in the patients with acromegaly. The maxillary sinus was only slightly smaller in the control group with a volume of 17.64 ± 4.19 cm³ (p = 0.2117). Furthermore, duration of clinical history (r = 0.028, p = 0.5134) and preoperative hormone levels (human GH r = 0.058, p = 0.7521; IGF-I r = 0.127, p = 0.4897) were not correlated with the maxillary sinus volume. However, a positive correlation between maxillary sinus volume and the variables tumor diameter (r = 0.374, p = 0.0348) and patient age (r = -0.474, p = 0.0061) was noted.

Volumetric analysis of the frontal sinus resulted in a statistically significant difference (p = 0.0382) between patients with acromegaly (14.89 ± 10.85 cm³; Fig. 5) and controls (10.06 ± 6.93 cm³). Within the group of patients with acromegaly, no statistically significant association of frontal sinus volume with duration of clinical history (r = 0.028, p = 0.8899) and tumor diameter (r = 0.266, p = 0.1418) was detected. A slight correlation was found between preoperative hormone levels and size of the frontal sinus (GH r = 0.289, p = 0.1089; IGF-I r = 0.342, p = 0.0554). However, this correlation did not reach statistical significance.

**Discussion**

Patients with acromegaly are characterized by a pathognomonic phenotype. The excess of human GH and IGF-I has ubiquitous effects on all tissues throughout the body. This excess results in the clinical features of acral enlargement, colon polyps, cardiovascular problems, sleep apnea, visceromegaly, and endocrine and metabolic alterations. In more than 95% of patients, acromegaly is derived from a pituitary adenoma.10

The shape and size of the head changes during the lifetime of not only patients with acromegaly, but also in healthy patients.3 Using lateral radiographs, Macho9 showed in his study of 353 patients that the viscerocranium increases up to the 4th decade of life and thereafter decreases, while the height of the neurocranium progressively decreases during an adult life. However, the effects of acromegaly on the patient’s head are much more striking. The viscerocranium is affected in terms of prognathism, malocclusion, maxillary widening, widened tooth gap, and nasal bone hypertrophy. At the neurocranium, the phenomenon of frontal bossing is well known because it gives a characteristic appearance to affected patients. Further, mucosal changes both in the nose and the paranasal sinuses in terms of mucosal hypertrophy and polypsis are reported occurrences in acromegaly.14

It is logical to assume that these morphological alterations have repercussions in microsurgical therapy. The transsphenoidal route is direct and safe for the majority of pituitary adenomas and thus represents the standard approach for pituitary surgery. In acromegaly, however, two issues related to the pathological anatomical alterations have to be taken into consideration when considering pituitary surgery.

First, the reduced intercarotid artery distance in the C5 and C4 segment narrows the habitual working space,4,12 increasing the risk of a potentially life-threatening vascular complication. Therefore, we have recommended bone window CT scan of the cranial base during preoperative diagnostics in patients with acromegaly scheduled for transsphenoidal surgery.4 In difficult cases, additional use of neuronavigation can be considered. Magnetic resonance imaging depicts the course of carotid arteries well. However, the chronic excess of human GH and IGF-I significantly distorts bone anatomy, which is better visualized by CT. Additionally, drilling of bone is often required for transsphenoidal exposure. Therefore, it is justified to add a CT scan to the preoperative workup. In acromegaly, it is important to know the position and proximity of the internal carotid arteries before surgery; even then, a very narrow intercarotid working space does not preclude the transsphenoidal intervention.4

Second, our data show that the anterior-posterior diameter of the sphenoid sinus is extended in patients with acromegaly compared with the control group. This diameter elongates the depth of the working corridor through the transsphenoidal route (Fig. 6). Saeki et al.13 studied morphological differences of the nasal cavity between patients with and without acromegaly and also found a narrower and deeper operating access in human GH-secreting adenomas. Osseous changes and pathological cartilaginous overgrowth of viscerocranium and neurocranium have implications for the selection of instruments for surgery.11

One-stage complete transsphenoidal resection is achievable in most pituitary adenomas. In selected cases, however, adenomas are more amenable to a trascranial approach. The degree of vertical intracranial extension as well as an irregular and multilobular configuration are important predictors of incomplete transsphenoidal resection.6 Pituitary adenoma removal is then performed through a

---

**Fig. 5.** Axial bone window CT scan shows an impressively enlarged frontal sinus in a patient with acromegaly.
Skull alterations in acromegaly

Author contributions to the study and manuscript preparation include the following. Conception and design: Ebner, Bültmann, Nägele, Honegger. Acquisition of data: Kürschnier. Analysis and interpretation of data: Ebner, Kürschnier, Honegger. Drafting the article: Ebner. Critically revising the article: Honegger. Reviewed final version of the manuscript and approved it for submission: Ebner, Nägele, Honegger. Statistical analysis: Dietz. Administrative/technical/material support: Ebner, Bültmann, Nägele, Honegger. Study supervision: Ebner, Honegger.

Acknowledgment

The authors thank Dr. F. Paulsen, Department of Radiooncology, Eberhard-Karls-University Tübingen, for professional and courteous advice regarding radiooncologic implications.

References


Address correspondence to: Florian H. Ebner, M.D, Department of Neurosurgery, Eberhard-Karls-University Tübingen, Hoppe-Seyler-Street 3, Tübingen, Germany 72076. email: florianebner@virgilio.it.

Conclusions

Significant craniometric changes and volumetric remodelling of the paranasal sinus occur in acromegaly. The bone alterations are of surgical importance for the transsphenoidal approach. Detailed preoperative diagnostic examination and planning as well as selection of appropriate instruments are mandatory for safe and successful pituitary adenoma removal in patients with acromegaly.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.