Developmental Abnormalities of the Skull Base in Patients with Turner Syndrome

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ABSTRACT: The skull base is one of the most complex anatomic structures of the skeleton that is responsible for protecting and supporting the brain and is also involved in the development of the facial structures. The main objective of our study was to evaluate skull base abnormalities in a group of patients diagnosed with Turner syndrome by assessing lateral cephalometric radiographs. A total of 7 patients diagnosed with Turner syndrome in the Endocrinology Department of the Emergency Clinical County Hospital of Craiova were included in the study. The following cephalometric variables were measured in our study: total skull base (N-Ba); Nasion (N)-Sella (S); anterior skull base (N-S): Nasion (N)-Sella (S); posterior skull base (S-Ba): Sella (S)-Basion (Ba). Regarding the investigated cephalometric variables, the mean±standard deviation (SD) recorded values in our study were 86.34±4.26mm for the total skull base (N-Ba), 63.87±2.54mm for the anterior skull base (N-S) and 38.33±4.87mm for the posterior skull base (S-Ba). The results of our study were compared to the ones provided by one of the most representative studies described in the literature. A reduced size of the posterior base of the skull is considered pathognomonic in subjects diagnosed with Turner syndrome. Also, the posterior base of the skull directly influences the maxillomandibular skeletal relationships and it is therefore necessary to calculate this cephalometric variable, which is easily highlighted on a lateral cephalometric radiograph.

KEYWORDS: Cephalometry, skull base, Turner syndrome.

Introduction

The skull base is one of the most complex anatomic structures of the skeleton that is responsible for protecting and supporting the brain and is also involved in the development of the facial structures.

In the latter case, the anterior base of the skull plays a central role due to its direct connection to the upper and middle face [1]. The base of the skull has different embryological origins.

Therefore, the anterior skull base develops from the neural crest alone, in a similar manner to the facial bones, while the posterior skull base develops from the paraxial mesoderm [1-3].

The base of the skull is formed through encondral ossification, in opposition to the craniofacial bones which are developed through intramembranous ossification.

The connection between the brain and the morphogenesis of the skull base has been studied for a long period of time.

Given the current knowledge, it seems that in the initial phase, the development and growth of the skull base is regulated by the brain, but this process still remains to be completely understood [1,4-10].

The relationship between the base of the skull and the dento-facial complex is also extremely important, mainly because pathologic growth and/or abnormal orientation of the skull base can lead to an abnormal position of both mandible and jaw in addition to an impaired mobility of these anatomical structures.

All these aspects indicate that the skull base is a unique structure due to its anatomical complexity and embryological development [11-22].

Aim

The main objective of our study was to evaluate skull base abnormalities in a group of patients diagnosed with Turner syndrome by assessing lateral cephalometric radiographs.

Material and Methods

The current study received approval from the local Ethics Committee.

The attending physician and the legal relatives of all the patients included in the study freely expressed their consent regarding the use of medical data for research purposes.

A total of seven patients diagnosed with Turner syndrome in the Endocrinology Department of the Emergency Clinical County Hospital of Craiova were included in the study.
The lateral cephalometric radiographs were performed with the help of a Carestream CS 8100SC device using the standard patient positioning represented by the perpendicular orientation of the X-ray beam on the patient’s sagittal plane.

Measurements of different cephalometric variables were performed by a single investigator.

Given that we performed linear and angular measurements, the results were expressed in millimeters and degrees.

The statistical processing of the measurements involved calculating the mean and standard deviation values.

The cephalometric points and reference lines for linear and angular measurements were marked on the lateral cephalometric radiographs (Figures 1 and 2).

The cephalometric points identified on a lateral cephalometric radiograph include:

- Nasion (N)-the most anterior point corresponding to the fronto-nasal suture;
- Point A-the most posterior point on the anterior contour of the upper jaw;
- Point B-the most posterior point on the anterior contour of the mandibular body, on the midline;
- Sella (S)-the rearmost opposite point of the quadrilateral blade;
- Basion (Ba)-the foremost point of the foramen magnum.

The following cephalometric variables were measured in our study:

- total skull base (N-Ba): Nasion (N)-Basion (Ba);
- anterior skull base (N-S): Nasion (N)-Sella (S);
- posterior skull base (S-Ba): Sella (S)-Basion (Ba).

We used IBM SPSS Statistics (version 20) for statistical calculations and the One-Way Analysis of Variance (ANOVA) test, considering a p value below 0.05 as statistically significant.

Figure 1. Cephalometric points and reference lines used for linear measurements: Nasion (N), Sella (S), Basion (B), Pterygo-maxillary point (Pm), Gnathion (Gn), Gonion (Go).
Figure 2. Labelled cephalometric points on a lateral cephalogram belonging to a male subject diagnosed with growth hormone deficiency: Nasion (N), Sella (S), Basion (B), Pterygo-maxillary point (Pm), Subspinale (Ss), Supramentale (Sm), Gnathion (Gn), Gonion (Go).

Results
Regarding the investigated cephalometric variables, the mean±standard deviation (SD) recorded values in our study were 86.34±4.26mm for the total skull base (N-Ba), 63.87±2.54mm for the anterior skull base (N-S) and 38.33±4.87mm for the posterior skull base (S-Ba) (Table 1).

A comparison between our study and the one conducted by Dumancic regarding the mean and SD values of these parameters is illustrated in Table 2.

Table 1. The mean and SD recorded values of the investigated cephalometric variables in our study.

| Variable                  | Mean   | SD  |
|---------------------------|--------|-----|
| Total skull base N-Ba (mm)| 86.34  | 4.26|
| Anterior skull base N-S (mm)| 63.87  | 2.54|
| Posterior skull base S-Ba (mm)| 38.33  | 4.87|

Table 2. A comparison between the results of our study and the results presented by Dumancic [23].

| Variable                  | The study performed by Dumancic | The current study |
|---------------------------|--------------------------------|------------------|
|                           | Mean   | SD  | Mean | SD  |
| Total skull base N-Ba (mm)| 93.07  | 6.01| 86.34| 4.26|
| Anterior skull base N-S (mm)| 63.52  | 3.83| 63.87| 2.54|
| Posterior skull base S-Ba (mm)| 36.90  | 3.11| 38.33| 4.87|
The values of N-Ba ranged between 75.27mm and 104.92mm in our study. Also, the values of N-S recorded in our study ranged between 54.90mm and 73.10mm, while the values of S-Ba ranged between 31.47mm and 49.22mm.

A comparison between our study and the one conducted by Dumancic regarding the minimum and maximum values of these parameters is illustrated in Table 3.

| Variable                        | The study performed by Dumancic Turner syndrome group | The current study |
|---------------------------------|-------------------------------------------------------|-------------------|
| Total skull base N-Ba (mm)      | Minimum: 82.50, Maximum: 111.63                      | Minimum: 75.27, Maximum: 104.92 |
| Anterior skull base N-S (mm)    | Minimum: 55.38, Maximum: 72.58                       | Minimum: 54.90, Maximum: 73.10  |
| Posterior skull base S-Ba (mm)  | Minimum: 30.93, Maximum: 48.29                       | Minimum: 31.47, Maximum: 49.22  |

We obtained a significant difference between the mean value of N-Ba provided by our study and the one provided by Dumancic (p<0.05).

However, the results of our study did not indicate any statistically significant differences between: (i) the mean value of N-S recorded in our study and the one obtained by Dumancic (p=0.580); (ii) the mean value of S-Ba provided by our study and the one obtained by Dumancic (p=0.356).

In our study, the mean value of the total skull base variable was lower than the mean value of the same variable presented by Dumancic in his study.

However, the mean value of the posterior skull base variable was slightly higher in our study.

The mean values of the anterior skull base variable were similar between the two studies.

**Discussions**

In patients with Turner syndrome, the shortening of the posterior skull base occurs mainly due to the X chromosome deficiency in craniofacial development in intrauterine life and in early childhood [23,24-27].

However, the anterior base of the skull may present a normal development in patients diagnosed with Turner syndrome given that this segment enlarges with the pneumatization and thickening of the frontal bone.

This usually happens at the age of six after the sphenoid-ethmoidal synchondrosis is closed.

Therefore, the evaluation of the skull base on a lateral cephalometric radiograph is extremely important due to the fact that the total skull base (N-Ba) and posterior skull base (S-Ba) appear to be shorter than in the normal population [23,25-33].

The study performed by Dumancic in his Turner syndrome group [23].

| Variable | Minimum | Maximum |
|----------|---------|---------|
| N-Ba     | 30.93   | 48.29   |
| N-S      | 55.38   | 72.58   |
| S-Ba     | 31.47   | 49.22   |
syndrome, craniosynostosis syndromes, cleido-cranial dysplasia etc.

In all these conditions, the skull base plays a central role in developing craniofacial abnormalities [43-48].

Recent studies indicate that growth hormone deficiency is associated with a reduced size of the skull base and face which results in malocclusions.

However, there seems to be no connection between craniofacial growth and teeth development.

Several studies evaluated the effects of growth hormone replacement therapy and most of the results indicated a difference in growth rate represented by a delayed development of the teeth compared to the craniofacial growth [49,50].

There are multiple dental pathological conditions secondary to growth hormone deficiency, which must be well documented and diagnosed.

After that, the most appropriate therapy is chosen in order to correct various pathological changes, some of which are related to growth hormone deficiency [51-54].

But the anomalies that appeared during the craniofacial growth and development process are not always caused by hormonal deficiencies, but can also be associated with genetic defects and low gestational weight [29,36,43,54].

All the previously mentioned aspects indicate the importance of the skull base in the facial growth and development.

Therefore, we consider the evaluation of the skull base and prognosis angles of the mandible and maxilla to be the most important cephalometric variables in highlighting craniofacial changes in patients diagnosed with Turner syndrome, in order to establish a correct diagnosis and apply an orthodontic suitable strategy.

Cephalometry is the most appropriate method in diagnosing and monitoring deficiencies in craniofacial growth and development in children with growth hormone deficiency.

Conclusions

A reduced size of the posterior base of the skull is considered pathognomonic in subjects diagnosed with Turner syndrome.

Therefore, there is a functional connection between the skull base and the dento-facial complex.

Also, the posterior base of the skull directly influences the maxillomandibular skeletal relationships and it is therefore necessary to calculate this cephalometric variable, which is easily highlighted on a lateral cephalometric radiograph.

Acknowledgments

Adina-Ioana Tecuta-Busoi and Marius Matei contributed equally to the manuscript and thus share main authorship.

Conflict of Interest

None to declare.

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