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Original Article

Cephalometric skeletal evaluation of patients with Incontinentia Pigmenti

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ABSTRACT

Purpose: The aim of this study was to evaluate the skeletal characteristics of patients with the rare genetic disease of Incontinentia Pigmenti, by lateral cephalometric analysis on the antero-posterior plane and by frontal cephalometric analysis on the horizontal plane.

Methods: Lateral skeletal cephalometric analyses were performed according to Steiner for evaluation of antero-posterior direction, and frontal skeletal cephalometric analyses according to Ricketts for evaluation of horizontal direction in 9 patients with IP. Left and right facial widths at the level of the zygomatic arch were also evaluated. The Student t-test was used for paired to a 5% level of significance data.

Results: The lateral skeletal cephalometric findings were not statistically significant, but the Class II was the most frequent finding (44.4%), followed by Class III (33.3%) and Class I (22.2%). The right maxillo-mandibular width was significantly lower than normal values, and the right facial width was significantly higher than the left, at the level of the zygomatic arch.

Conclusions: Patients with IP showed more skeletal discrepancies of Class II and III than Class I malocclusion, and had significant horizontal facial skeletal asymmetries. This should alert health professionals to route these patients for orthodontic assessment and possible therapeutic interventions. However, larger samples are needed to better elucidate if these cephalometric findings can be specifically related to IP.

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1. Introduction

In 1926, Bloch reported a case with characteristics of Incontinentia Pigmenti (IP),¹ and a year later, Sulzberger published a detailed description of this case, besides observing that it is restricted to females.² Therefore IP became known also as Bloch–Sulzberger syndrome, it was described for the first time by Garrod in 1906. It is a rare genetic syndrome³ which is linked to the X chromosome, with a dominant inheritance mode.⁴ Most cases are sporadic (>65%), but may be of familial origin.³ It is usually lethal for male fetuses, still in the intra-uterine period, and the disease has an approximate incidence of 1:40.000 girls.⁴ However, there are reports of situations in which boys can show IP, which would be when they present mosaicism for the disease,⁵ or are carriers of Klinefelter syndrome,⁶ which is characterized by the presence of an extra X chromosome (47, XXY).⁷ In the pathogenesis of IP, there is generally a mutation that inactivates the *gamma* *IKK* gene, also called NEMO, mapped to Xq28 (region 28 of the long arm of the X chromosome).⁸

IP is a condition that can show anomalies in the ectoderm of different organs and tissues. However, the mesoderm can also be altered causing skeletal and cardiac abnormalities.³ Cutaneous lesions are considered the main findings of IP⁹ and usually appear at birth or soon after and manifest by four different stages,¹⁰ which evolved from vesicular or erythematous lesions to linear hypopigmented patches with or without skin atrophy.⁸ Treatment is only symptomatic.¹¹ Changes in the central nervous system can also occur,^{4,8,9} as seizures and mental retardation. Among the others signs and symptoms found are syndactyly, spina bifida, nasal dystrophy and anomalies in the scalp such as fine hair and alopecia.⁴

The stomatognathic system includes as basic components the bones of the cranium and face, the teeth and their support elements, temporomandibular joint (TMJ) and the masticatory and facial expression muscles,¹² and there are published reports of clinical cases of patients with IP who show some alterations in this system.^{13,14} The skeletal problems described in the literature were transverse unilateral discrepancy of the maxilla associated to oligodontia in the maxilla and mandible,¹³ skeletal Class III malocclusion with protruding chin on clinical examination¹⁴ and facial asymmetries,^{15,16} such as hemifacial hypoplasia.¹⁷ Dental anomalies¹⁶ occur in 80% of IP cases⁸ and affect both the deciduous and permanent dentition, with the latter more so.¹⁴ Tooth agenesis, conical teeth with extra cuspids in the posterior teeth and delay in tooth eruption with missing teeth are the most common anomalies described.¹⁶ Besides, bad tooth positions and loss of the vertical dimension of occlusion associated to missing teeth can occur.¹⁴ Some patients present with disturbances in formation of the tooth enamel,¹⁸ with many caries.¹³ These dental characteristics of IP can be confused with other congenital diseases such as congenital syphilis and ectodermal dysplasia. But there are subtle differences in the morphology of the teeth that distinguish these disturbances, together with the laboratory, characteristic cutaneous lesions and other systemic manifestations.⁴ Cleft lip and palate,^{4,8,9} ogival palate, and hypoplasia of the soft

palate can also occur.^{8,9} Additionally, patients can show alterations in orofacial motricity and deglutition,¹⁹ and speech problems.⁸

IP is considered a congenital etiological factor of malocclusion, because the dentofacial deformities are among its signs and symptoms, making the study of these patients important for orthodontics.¹⁵ Cephalometric analyses contribute to the diagnosis of dentofacial deformities and have advantages such as easy access, low cost and little radiation.²⁰ Thus, the objective of this study was to evaluate the skeletal characteristics of patients with IP, by lateral cephalometric analysis on the antero-posterior plane and by frontal cephalometric analysis on the horizontal plane.

2. Methods

Initially, 16 patients diagnosed with IP according to the criteria of Landy and Donnai²¹ were selected among the children seen at the Pediatric Dermatology Service of the Hospital da Criança Santo Antônio, Porto Alegre, Brazil, between 2003 and 2012. All patients or their parents/guardians gave signed informed consent. Included in the study were 9 patients who met the necessary requisites to be subjected to lateral cephalometric analyses as proposed by Steiner²² and frontal cephalometric analyses as proposed by Ricketts.²³ Among these requisites, the patients had to have permanent upper and lower incisors erupted, delimiting the anterior edge of the maxilla and mandible to allow lateral cephalometric tracings to be done with the selected skeletal measurements, from the cephalogram according to Steiner.²² In addition, they had to have the minimal ages recommended by Ricketts²³ for comparison of the frontal skeletal cephalometric measurements selected for this study with the frontal cephalogram of the author with its normal values serving as a reference. Frontal and lateral telerradiographs, both analog and digital, were requested in the same radiology center for all patients. These were obtained by the conventional method of positioning the head using the auricular positioner of the cephalostat and Frankfurt horizontal plane parallel to the floor, where the analog radiographs were acquired with Sirona Orthophos (Germany) radiological equipment, and the digital radiographs with Sirona Orthophos XG (Germany) instruments. The lateral and frontal cephalometric tracings were done manually on the analog radiographs, all by the same operator (author of this study) and in the same data. Acetate tracing paper 0.003 matte finish of 8 × 10 inches (G&H Wire Company, USA) was utilized, which was affixed to the telerradiographs with 12 × 10 mm Scotch tape (3M, USA), on the top and left sides. The cephalometric tracings were made in a dark room on a negatoscope (VH Soft Line, Brazil), with the help of a Unitek tracing template (3M, USA), 0.9 mm graphite pencil (Pentel, Japan) and soft eraser (Faber Castell, Brazil). The measurements utilized, selected from the cephalograms of the above-cited authors, were the angular lateral skeletal cephalometric measurements²² SNA, SNB and ANB (Fig. 1) utilizing the interpretations of Tweed²⁴ for diagnosing skeletal malocclusions of Class I (ANB between zero and 4.5°), Class II (ANB greater than 4.5°), and

Fig. 1 – Lateral cephalometric tracing.

Fig. 2 – Frontal cephalometric tracing.

Class III (ANB less than zero); and the frontal skeletal cephalometric measurements²³ (Fig. 2): left maxillo-mandibular width – LMME (distance from line ZL-AG to point JL), right maxillo-mandibular width – LMMD (distance from point JR to line ZR-GA), the maxilla transverse distance – DTMx (distance between points JL and JR), the mandible transverse distance – DTMd (distance between AG and GA), nasal width – LN (distance between NC and CN), total facial width – LFT (distance between ZA and AZ), maxillary symmetry (SMx) – deviation of the maxilla (point ASN) towards the right or left side in relation to middle vertical line (CG-Me) and mandibular symmetry (SMd) – deviation of the mandible (point Pog) toward the right or left side in relation to middle vertical line (CG-Me), where a negative value would indicate a deviation to the left and a positive value to the right, and total facial width (LFT) from the left zygomatic arch point (ZA) to the right zygomatic arch point (AZ). Besides these, two additional measurements were evaluated, which were utilized to determine the existence of some transverse facial asymmetry at the level of the zygomatic arch, where in the visual analysis of the frontal telerradiographs the right side appeared to be wider than the left side in the majority of patients. These were the left facial width (LFE), measured from ZA to the middle vertical line (CG-Me), and the right facial width (LFD), measured from the middle vertical line (CG-Me) to the point AZ. In the normality, both measurements should have the same value. In all patients in who the frontal cephalometric measurements of Ricketts²³ were utilized, the convention of age only in years was utilized, as presented in his tables of normal values, so that the frontal skeletal cephalometric values could be compared with the values of this author. Therefore, in those who had “x” years and “y” months, when the “y” months were upto 6 months, the age of “x” years was utilized, and when the “y” months were more than 6 months, the next age that the patient would be was utilized. By this convention, only one patient was 1 year and 3 months below (7 years and 9 months) the minimal age of 9 years for the normal value recognized by Ricketts²³ for measurement of “transverse distance of the maxilla (DTMx)”. In this case, 0.6 mm was subtracted from the normal value for 9 years of age to obtain that would be the value normal in about 8 years of age, where the maxilla grows 0.6 mm per year in the transverse direction, according to the author. This was an observational cross-sectional study, and was approved by the Committee of Ethics and Research of the Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA).

Data processing was done by creating a databank in the program SPSS version 12.0 for Windows, and statistical analysis was carried out by descriptive statistics utilizing the Student t-test for paired to a 5% level of significance data.

3. Results

Among the 9 patients of the sample who fulfilled the clinical and cephalometric criteria for inclusion in the study, all were female and of European descent, with ages between 7 years and 9 months and 33 years and 7 months (mean of 20 years and 3 months and standard deviation of 10 years and 6

Table 1 – Comparison with reference values.

Measurement	Study group		<i>p</i>	Result
	Mean	SD		
SNA	83.06	3.86	<i>p</i> > 0.05	Normal
SNB	80.17	3.61	<i>p</i> > 0.05	Normal
ANB	2.89	4.01	<i>p</i> > 0.05	Normal
LMMD	7.50	2.94	<i>p</i> < 0.05	Less than normal ^a
LMME	9.22	4.25	<i>p</i> > 0.05	Normal
DTMx	64.94	9.47	<i>p</i> > 0.05	Normal
DTMd	78.89	5.88	<i>p</i> > 0.05	Normal
LN	27.00	3.31	<i>p</i> > 0.05	Normal
SMx	+0.66	+1.17	<i>p</i> > 0.05	Normal
SMd	+0.10	+0.73	<i>p</i> > 0.05	Normal
LFT	122.22	5.04	<i>p</i> > 0.05	Normal

SD: standard deviation.
^a Significant difference in relation to normal values, at 5% level of significance.

months). Two patients are sisters and two are mother and daughter.

On the basis of the Student *t*-test for paired data, the cephalometric measurement LMMD in the sample investigated was significantly lower than normal values (*p* < 0.05, Table 1), and LFD values were significantly higher than the LFE values (*p* < 0.05, Table 2).

The lateral and frontal cephalometric findings in frequency (%) can be respectively seen in Figs 3–5.

4. Discussion

In this study, the skeletal pattern of the patients, although not statistically significant and a small sample, draws attention to 44.4% had Class II, 33.3% had Class III, and only 22.2% had Class I, in which there is harmony between the maxilla and mandible. The presence of Class III is in accordance with cases of IP reported in the literature,^{11,14} however in this sample, the most patients had Class II (44.4%) and maxillary prognathism (66.7%). However, there is some criticism about the ANB angle, which can change when the base of the cranium is short or the maxilla and/or mandible is rotated. There are proposals from other authors for this evaluation, such as the analysis of Wits, which relates their points A and B with the occlusal plane and not the maxilla and mandible with the cranium.²⁵ Since

Table 2 – Comparison between the measurements LFE and LFD.

Measurement	Study group		<i>p</i>	Result
	Mean	SD		
LFE	59.22	3.11	<i>p</i> < 0.05	LFD values significantly higher than LFE values ^a
LFD	62.94	2.92	–	

SD – standard deviation.

^a Significant difference between the measurements LFE and LFD, at 5% level of significance.

Fig. 3 – Lateral cephalometric findings in frequency (%) (Prog. – Prognathia; Retro. – Retrognathia).

missing teeth are common in patients with IP,¹⁶ Wits' analysis would not be indicated, because the determination of the occlusal plane is hampered. Even though having faults as well, the use of telerradiography in the dento-skeletal evaluation of the patients complements subjective clinical evaluation. It is noteworthy yet that 2 of the 9 members of the sample were utilizing a permanent orthodontic device, which may have led to some alteration of points A and B due to the inclinations acquired by the incisors. For example, an inclination of the more palatal root of an upper incisor may move the point A posteriorly. However, no dental cephalometric or vertical skeletal measurement was utilized in this study, because they are influenced by tooth positioning.

The right maxillo-mandibular width was significantly lower than the normal value recognized by Ricketts,²³ indicating that there was some facial asymmetry in these patients, in concordance with some authors who described facial asymmetries in patients with IP.^{15,16} This alteration can be related to factors such as the widths of the maxilla and mandible, where although not significantly altered in this sample. The deviation of the maxilla in 88.9% of patients (with a mean of 0.66 mm) and of the mandible in 55.6% of patients (with a mean of 0.10 mm), both to the side right, which although small could also contribute. However, mandibular deviation can be caused by dental interference not evaluated in this study. The position of the left (ZL) or right (ZR) frontal zygomatic arch point and of the left (AG) and right (GA) antegonial points that comprise the left (ZL-AG) or right (ZR-GA) frontal facial line utilized as reference in this measurement can also be related. In addition, the right facial width was significantly larger than the left facial width, at the level of the zygomatic arch, indicating facial asymmetry also at a higher level of the face of these patients with IP.

Some authors report nasal dystrophy in patients with IP,^{4,15} and in this study nasal width was measured to determine any transverse atresia. On average, the values were within normal, but 88.9% of the patients showed this width decreased, albeit by not more than 2.5 mm. Analyzing each patient individually, only one showed this measurement to be increased, by only 0.5 mm. Furthermore, in this sample total facial width at the level of the zygomatic arch was decreased

Fig. 4 – Frontal cephalometric findings in frequency (%).

Fig. 5 – Frontal cephalometric findings in frequency (%).

in 77.8% of patients, although the mean value was not significantly lower than normal; still, in one of the patients this parameter was 21.8 mm less than normal.

LFD values were significantly higher than LFE values in this study. Although there are reports in the literature of facial asymmetries,^{15,16} such as hemifacial hypoplasia,¹⁷ we cannot affirm that in this sample there was facial hypoplasia of the left side or facial hyperplasia of the right side at the level of the zygomatic arch, because to make this differential diagnosis, we would need the reported normal values and standard deviations for LFD and LFE in patients with a normal skeletal pattern at each age to allow comparison. Accordingly, it would not suffice to divide the normal value of LFT by two for each age.

disclosed that skeletal facial asymmetries in the horizontal direction may be frequent in IP. However, further studies with larger samples are needed to confirm that these cephalometric findings are specifically related to IP. This study warns that professionals who have contact with IP patients could advise them to undergo a complete orthodontic research at the appropriate time in order to assess possible therapeutic needs. These may be of orthodontic, orthopedic and/or surgical order, depending on the patient age, the problem and its intensity.

Conflicts of interest

All authors have none to declare.

5. Conclusions

The lateral cephalometric analysis of the patients with IP demonstrated a possible presence of skeletal discrepancies in the antero-posterior direction more in Classes II and III than Class I malocclusion. The frontal cephalometric analysis also

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