Cephalometric findings in patients with Papillon-Lefèvre syndrome

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Introduction: Literature regarding oral conditions in patients with Papillon-Lefèvre syndrome (PLS) often covers the periodontal aspects, but no literature was found describing specific craniofacial findings in this group. The aim of this retrospective study was to investigate the cephalometric findings of patients with PLS. **Methods:** Lateral cephalograms of 8 patients with PLS were traced, and hard- and soft-tissue variables were analyzed. **Results:** Class III skeletal relationship was evident (ANB angle, 2° ± 3.1°; Wits appraisal, −9.1 mm ± 3.7 mm). Other findings include maxillary retrognathia, decreased lower facial height, retroclined mandibular incisors, and upper lip retrusion. **Conclusions:** Patients affected with PLS have a Class III skeletal pattern. These findings can be of clinical value not only for diagnosis, but also for proper treatment planning. (Am J Orthod Dentofacial Orthop 2008;134:138-44)

Papillon-Lefèvre syndrome (PLS) is an autosomal recessive disorder. The 2 cardinal diagnostic features of the syndrome are palmoplantar keratosis and an early-onset form of aggressive periodontitis.[1] The palms and soles have a dry, red, and scaly appearance. Other areas, including cheeks, eyelids, labial commissures, legs, thighs, knees, and elbows, can be affected by the keratosis, although it varies significantly.[1] Ullbro et al[2] studied 47 patients with PLS and found no significant correlation between the severity of the skin lesions and the level of periodontal infection. Before tooth eruption, the gingival and mucosal surfaces appear normal. As the skin lesions appear, the gingiva becomes inflamed and swollen. Rapid periodontal destruction occurs as teeth erupt. In many uncontrolled situations, most of the primary dentition is lost by age 4 or 5 years, followed by loss of the permanent dentition in the early teens.[1] Histologic examination of extracted teeth from 2 affected persons showed areas of root resorption of various depths and extents, signs of spontaneous repair, and areas with healthy cementum.[3]

An extensive review of the literature showed that most studies of PLS focused on the genetic basis[4-10] and the periodontal management of the syndrome.[11-18] The gene responsible for PLS was mapped to chromosome 11q14-q21.[19] Periodontal literature shows that it is possible to successfully maintain a healthy periodontium in these patients with early treatment and preventive measures.[15,20] This includes oral hygiene instructions, use of mouth rinse, frequent debridement, multiple antibiotic regimens, periodontal surgery, and extraction of hopeless teeth.[11] An isolated case report of PLS presented the combined periodontal-orthodontic management of a patient aged 7 years 9 months.[21] A stable periodontal situation was achieved after 26 months of combined mechanical and antibiotic therapy. This initial therapy was followed by orthodontic treatment with fixed appliance without further pronounced periodontal deterioration. Spaces for eruption of the canines and the premolars were created, in addition to the alignment of teeth. In another case report, a lingual holding arch was placed on the first molars once they erupted.[11] Until now, no article has described the craniofacial features of patients with PLS.

Our clinical observation is that patients with PLS have the characteristics of Class III skeletal malocclusion. Our aim in this study was therefore to establish a cephalometric baseline for skeletal and soft-tissue variables in PLS patients.

MATERIAL AND METHODS

Patient records at King Faisal Specialist Hospital and Research Center (KFSH & RC) in Riyadh, Saudi Arabia, were used for this study. There were 47 patients

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Submitted, March 2007; revised and accepted, January 2008.
0889-5406/$34.00

doi:10.1016/j.ajodo.2008.01.002

(26 female, 21 male) with the diagnosis of PLS in the PLS database.

Only subjects with occlusal stops (at least 1 occlusal molar contact with the opposing arch) were chosen for this study. The periodontal condition of the molars in occlusion was evaluated by a consultant periodontist (C.U.) and found to be in a controlled healthy condition. Patients with no occlusal stops were excluded, since they do not have a reproducible occlusion, and their sagittal and vertical relationships could be misleading.

From the 47 patients with PLS, and based on the inclusion criteria of posterior occlusal stops, 8 adolescents were included in this study. Their ages ranged from 12 to 19 years (mean, 16 years); there were 4 boys and 4 girls.

The lateral cephalometric radiographs used in this study were from the database at KFSH & RC with the following standard protocol. The patient was seated in a chair with the head in a natural position. A lateral skull radiograph was taken with the teeth in centric occlusion and the lips at rest. The magnification factor was 0.9. All radiographs were taken with the same unit (cephalostat, B. F. Wehmer, Addison, Ill) at 75 kV(p), 15 mA, and an exposure time of 1 second. The use of these records for research was approved by the Research Center Committee at KFSH & RC.

Each radiograph was hand traced on acetate paper. All tracings were performed by an author (N.B.). Linear and angular measurements were measured to the nearest 0.5 mm and 0.5°, respectively.

Angular and linear measurements were calculated for the hard and soft tissues. All reference points are shown in the Figure.

The error of the method of the skeletal, dental and soft-tissue cephalometric measurements was calculated by means of double determination. All cephalometric radiographs were retraced, and all landmarks and measurements were repeated twice 2 weeks later. Dahlberg's formula[22] was used to calculate the measurement error. All errors measured were insignificant. The lowest error 0.19 mm for the lower lip to esthetic line measurement, and the highest error was 1.19° for the nasolabial angle measurement. The mean error for linear measurements was 0.43 ± 0.19, while angular measurements was 0.88° ± 0.27°.

Statistical analysis

These data were subjected to statistical tests with SPSS statistical software (SPSS, Chicago, Ill). Descriptive statistics (mean, standard deviation, and range) were calculated from the observed values of each measurement. Pearson correlation was used to determine any significant correlations between the variables up to the .01 and .05 levels of significance.

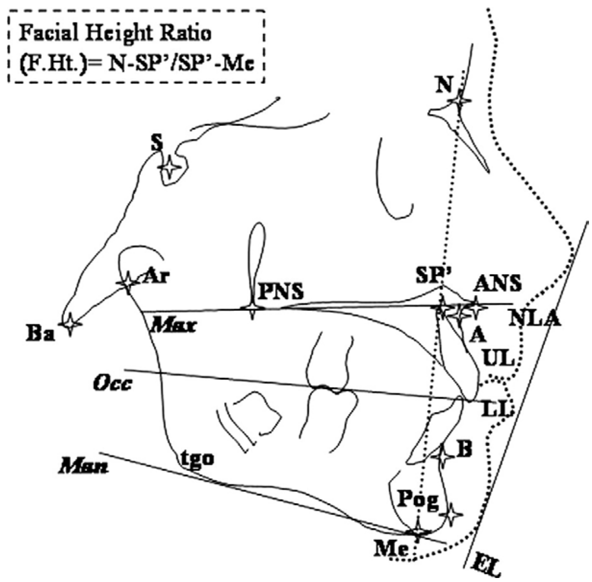

Fig. Cephalometric landmarks and their definitions: articulare (*Ar*); basion (*Ba*); sella (*S*); nasion (*N*); Point A; spine point marked (*SP'*): intersection of N-Me line and Max plane; Point B; pogonion (*Pog*); menton (*Me*); most anterior point of upper lip (*UL*); most anterior point of lower lip (*LL*); mandibular plane (*Man*): a line connecting Me and gonion tangent (*tgo*); maxillary plane (*Max*): a line connecting the anterior and posterior nasal spines (*ANS* and *PNS*, respectively); occlusal plane (*Occ*): line passing through the occlusal table at the molar and premolars areas; AB line: line from Point A to Point B; esthetic line of Ricketts (*EL*): a tangent from the tip of the nose to the chin; nasolabial angle (*NLA*).

RESULTS

The means, standard deviations, and minimum and maximum values of the hard- and soft-tissue findings are shown in Table I. The ANB angle, Wits appraisal, and Occ-AB indicate a skeletal Class III relationship (see Fig for abbreviations). The skeletal profile was concave with decreased lower facial height. Maxillary length (Ar-A) was decreased. The mandibular incisors were retroclined, mean overjet was decreased, and all patients had varying degrees of upper lip retrusion.

Variables indicating skeletal Class III relationship were shown to have statistically significant correlations to each other. ANB angle was correlated significantly to the Wits appraisal, and the Wits value was correlated significantly to ANB angle and Occ-AB plane. This supported the Class III pattern for these patients. When ANB angle was correlated to the mandibular and

Table I. Descriptive statistics

	Minimum	*Maximum*	*Range*	*Mean*	*SD*
SNA (°)	67.5	85.0	17.5	76.4	6.2
SNB (°)	73.50	86.00	12.50	78.4	4.3
ANB (°)	−6.50	2.00	8.50	−2.0	3.1
Wits (mm)	−15.00	−4.00	11.00	−9.1	3.7
Occ-AB (°)	70.00	84.00	14.00	77.2	5
SNPog (°)	76.00	87.00	11.00	80.2	4.1
NAPog (°)	−18.00	4.50	22.50	−7.4	7.5
SNBa (°)	121.00	141.00	20.00	133.1	6.1
Man-SN (°)	30.00	44.50	14.50	37.8	5.3
Max-SN (°)	8.00	18.00	10.00	11.8	3.1
Occ-Max (°)	6.00	17.00	11.00	10.1	3.6
Max-Man (°)	20.00	33.50	13.50	26.0	4.8
Me-tgo-Ar (°)	121.00	136.00	15.00	129.0	5.2
N-SP' (mm)	52.00	57.00	5.00	53.6	5
SP'-Me (mm)	58.00	75.00	17.00	65.1	6.3
F Ht (%)	74.00	89.70	15.70	82.8	6.1
Ar-A (mm)	74.5	94	19.5	80.87	6.43
Ar-Pog (mm)	99	128.5	29.5	107.7	9.94
OJ (mm)	−0.5	1.5	2	0.43	0.93
⊥-⊤ (°)	120.00	154.00	34.00	136.8	14.3
⊥-Max (°)	104.50	125.50	21.00	115.3	8.3
⊥-NA (°)	18.00	31.50	13.50	26.3	4.5
⊥-NA (mm)	3.50	8.00	4.50	5.4	1.8
⊤-Man (°)	68.00	89.00	21.00	81.0	9.2
⊤-NB (°)	7.00	30.50	23.50	17.5	10.0
⊤-NB (mm)	−1.00	5.50	6.50	2.0	2.5
⊤-APog (mm)	−.50	5.00	5.50	2.1	2.1
Pog-NB (mm)	−.50	5.50	6.00	3.4	2.2
UL-EL (mm)	−13.50	−3.00	10.50	−7.0	3.3
LL-EL (mm)	−6.00	1.00	7.00	−3.1	2.5
NLA (°)	39.00	110.00	71.00	86.0	22.1
Age (y)	12	19	7	16.0	—

F Ht, Facial height; *OJ,* overjet; ⊥, upper incisors; ⊤, lower incisors.

Table II. Correlations of the maxilla and mandible in the sagittal plane

	SNB angle	*ANB angle*	*Wits*	*Occ-AB*
SNA Pearson correlation	.878†	.755*	.414	.280
Significance (2-tailed)	.004	.030	.308	.501
n	8	8	8	8
SNB Pearson correlation		.249	−.003	−.105
Significance (2-tailed)	—	.397	.995	.805
n		8	8	8
ANB Pearson correlation			.814*	.693
Significance (2-tailed)	—	—	.014	.057
n			8	8
Wits Pearson correlation				.911†
Significance (2-tailed)	—	—	—	.002
n				8

*Correlation is significant at the .05 level.
†Correlation is significant at the .01 level.

Table III. Correlations of facial height (F Ht) with maxillary and mandibular plane inclination

	N-SP'	*SP'-Me*	*Man-SN*	*Max-SN*
F Ht				
Pearson correlation	−.446	−.940†	.290	.759*
Significance (2-tailed)	.268	.001	.485	.029
n	8	8	8	8
N-SP'				
Pearson correlation		.721*	−.063	−.626
Significance (2-tailed)	—	.043	.883	.097
n		8	8	8
SP'-Me				
Pearson correlation			−.263	−.822*
Significance (2-tailed)	—	—	.529	.012
n			8	8
Man-SN				
Pearson correlation				.414
Significance (2-tailed)	—	—	—	.308
n				8

*Correlation is significant at the .05 level.
†Correlation is significant at the .01 level.

maxillary position relative to the cranial base, only the SNA angle showed a significant relationship. Table II shows the correlations of these variables.

The facial height ratio was increased and found to correlate negatively ($P < 0.01$) to lower facial height. However, upper facial height did not have a significant correlation. A significant correlation between facial height and the inclination of the maxilla to anterior cranial base was also evident from the results (Table III).

Table IV illustrates the correlations between the soft- and hard-tissue variables. The position of the upper lip correlated significantly ($P < 0.05$) to the inclination of the mandibular incisors to the mandibular plane. Lower lip position did not correlate significantly to the position of the mandible indicated by SNPog. Nevertheless, it was correlated significantly to the inclination of the maxillary incisor to the maxillary plane and to the mandibular incisor position to APog. The mandibular incisor inclination to the mandibular plane had a significant correlation to the ANB angle.

Table V gives the comparisons between our data and previous studies of Saudi norms for skeletal Class I subjects.[23,24] The data of the skeletal Class I subjects was used as the control for confirming our results. There were significant differences for SNA, ANB, and NAPog. Also, significant differences for dental variables were found for interincisal angle and mandibular incisor to NB line (linear and angular measurements). Linear measurement of the maxilla (Ar-A) was significantly decreased ($P < 0.01$), whereas the mean of mandibular length (Ar-Pog) did not show a significant difference on comparison. Nasolabial angle and the

Table IV. Soft-tissue correlations

	LL-EL	*⊥-Max*	*⊤-Man*	*⊤-APog*	*SNPog*	*ANB*
UL-EL Pearson correlation	.835†	.780	.907*	.538	−.106	.606
Significance (2-tailed)	.010	.067	.034	.350	.802	.111
n	8	6	5	5	8	8
LL-EL Pearson correlation		.871*	.806	.884*	−.237	.261
Significance (2-tailed)	—	.024	.100	.047	.572	.532
n		6	5	5	8	8
⊥-Max Pearson correlation			.885*	.777	.261	.472
Significance (2-tailed)	—	—	.046	.122	.617	.345
n			5	5	6	6
⊤-Man Pearson correlation				.489	.244	.937*
Significance (2-tailed)	—	—	—	.403	.693	.019
n				5	5	5
⊤-APog Pearson correlation					.274	.486
Significance (2-tailed)	—	—	—	—	.655	.407
n					5	5
SNPog Pearson correlation						.250
Significance (2-tailed)	—	—	—	—	—	.550
n						8

⊥, Upper incisors; ⊤, lower incisors.
*Correlation is significant at the .05 level.
†Correlation is significant at the .01 level.

Table V. Comparision between the study sample and norms for the Saudi population

	Saudi norms‡		*Present study*			
Variable	*Mean*	*SD*	*Mean*	*SD*	*T value*	P *value*
SNA (°)	83.41	5.28	76.438	6.150	3.05†	<0.01
SNB (°)	80.71	4.74	78.4375	4.3048	1.19	>0.1
ANB (°)	2.71	1.58	−2.0000	3.1396	5.48†	<0.001
SNPog (°)	81.80	4.54	80.1875	4.0878	0.88	>0.1
NAPog (°)	3.00	3.65	−7.4375	7.4854	5.17†	<0.001
Ar-A (mm)	85.84§	3.91§	80.87	6.43	3.11†	<0.01
Ar-Pog (mm)	107.17§	4.46§	107.7	9.94	−0.26	>0.1
T-⊥ (°)	122.96	9.63	136.800	14.2680	−3.06†	<0.01
⊥-NA (°)	24.76	6.10	26.2500	4.5028	−0.62	>0.1
⊥-NA (mm)	5.98	2.89	5.4167	1.7725	0.51	>0.1
T-NB (°)	29.46	4.87	17.5000	10.0437	4.41†	<0.001
T-NB (mm)	6.50	2.66	2.0000	2.5249	4.13†	<0.001
UL-EL (mm)	−4.00	3.19	7.0000	3.2842	2.26*	<0.05
LL-EL (mm)	−1.02	3.13	−3.0625	2.5275	1.66	>0.1
NLA (°)	103.59	11.13	86.0000	22.1085	2.90†	<0.01

⊥, Upper incisors.
*Correlation is significant at the .05 level.
†Correlation is significant at the .01 level.
‡Data from Hashim.[23]
§Data from Alnamankani.[24]

position of the upper lip to the esthetic line showed significant differences as well.

DISCUSSION

The literature contains many articles describing the cephalometric characteristics of patients affected with syndromes, such as Down,[25] Marfan,[26] Apert,[27] Pierre Robin,[28] and others.[29-32] No published report describing the cephalometric findings or the craniofacial characteristics of patients with PLS was found in the literature.

The prevalence of PLS is reported to be 1 to 4 cases per million.[33] When this was extrapolated to the population of Saudi Arabia (26 million), a reasonably large sample size was found as the initial study sample (47 patients). The incidence of PLS might be higher in the Saudi population. However, this could not be confirmed from the literature.

Our sample contained siblings. Two siblings, along with another 3 siblings, were descended from 2 families. Although not all of the 47 patients were included in our study, all siblings shared the same dentofacial pattern of the original sample. Their skeletal features were also similar to the rest of the studied subjects. However, studies with more patients from autonomous families are needed to further support these findings.

All ANB-angle measurements indicated a Class III skeletal relationship with a mean of −2°, except in 2 subjects. In 1 of these subjects, the ANB angle showed a Class III skeletal relationship after adjustment of anterior cranial base (S-N) to the Frankfort horizontal plane. Although the other subject had an ANB angle indicating a Class I relationship, a Class III sagittal relationship was evident from other variables (Wits appraisal, −6 mm; Occ-AB, 81°).

The Wits and Occ-AB variables indicated a skeletal Class III relationship, with means of −9 mm and 77°, respectively. These variables (ANB, Wits, and Occ-AB) correlate significantly to each other, indicating a true interpretation of each one. As reconfirmation of the Class III skeletal relationship, the NAPog showed skeletal concavity with a mean score of −7.4° (Table I).

Overjet was decreased (−0.5-1.5 mm). Most subjects had an edge-to-edge relationship. Only 2 showed a positive value (1.5 mm). However, they demonstrated a clear skeletal Class III relationship as indicated by the Wits analysis (−6 mm and −4 mm). The mandibular plane showed backward rotation in relation to the cranial base (41° and 39°); this might have contributed to the relatively increased overjet.

SNA angle correlated significantly to the ANB angle, but SNB angle did not (Table II). This implies that the cause of the skeletal Class III relationship is related to a retrognathic maxilla rather than a prognathic mandible. Not only was the maxilla retrognathic, but also the maxilla was found to be hypoplastic, as indicated by the decreased value of its linear measurement (Ar-A). Other syndromes that share the feature of maxillary hypoplasia include Cohen[34] and Crouzon.[35] Naidoo et al[36] demonstrated maxillary vertical deficiency along with horizontal underdevelopment in patients with fetal alcohol syndrome. Also, those with Binder's syndrome were reported to have horizontal underdevelopment of the maxilla.[37] Early loss of the maxillary deciduous dentition is common in patients with PLS.[1] It is not yet clear, or reported, whether this early loss play a role in the normal growth and development of the maxilla. However, it is a clinical experience that early loss of either the deciduous or the permanent teeth will cause loss of alveolar bone in both the vertical and horizontal dimensions, and many patients with PLS develop a Class III relationship.

The sample showed decreased lower facial height, similar to that observed in many skeletal Class III patients. Table III shows a significant correlation between the facial height ratio and the maxillary plane. Therefore, lower facial height was decreased in this sample mainly because of posterior (clockwise) inclination of the maxillary plane. The relatively small nasolabial angle also added to the Class III characteristics of affected patients.

As is usually seen in skeletal Class III relationships, the mandibular incisors tend to be retroclined as dental compensation for the skeletal discrepancy. In this sample, the mandibular incisor inclination to the mandibular plane was decreased and correlated significantly with the decrease in the ANB angle (Table IV).

In Class III malocclusion, the mandibular incisors are usually positioned in front of the maxillary incisors in the sagittal plane. This relationship allows the mandibular anterior teeth to influence the position of the maxillary incisors. This anterior dental relationship and the resultant axial inclination also control the position of the upper and lower lips. That was reflected in this study as a significant correlation between the retruded upper lips and the retroclination of the mandibular incisors to the mandibular plane (Table IV). The mandibular incisors were retruded in relation to the A-Pog line. That position influenced the lower lip and showed a significant correlation (Table IV).

Our data were compared with Saudi normal cephalometric readings to confirm our findings statistically. Previous studies for determining normal cephalometric findings for Saudi men were used for this purpose.[23,24] The comparison showed statistically significant differences for ANB, NAPog, and SNA. The Saudi norm for SNA is 83.41°; for patients with PLS, this was 76.44°. Furthermore, the maxillary length of subjects with PLS was significantly decreased compared with Saudi norms. Unlike the Ar-A measurement, the Ar-Pog measurement did not show a significant difference on comparison. This finding, along with the significantly decreased SNA angle, further confirms the association of a Class III pattern in our sample, with the maxilla both hypoplastic and retrognathic in the sagittal dimension. The inclination of the mandibular incisor also showed a significant difference; it was more retroclined in patients with PLS as a result of dental compensation. Differences regarding soft tissues were evident for upper lip position; it was more retrusive, and NLA was more acute in patients with PLS.

Orthopedic correction is a documented approach in the literature for early correction of mild skeletal Class III discrepancy.[38,39] Typically, this requires stable and healthy dental and periodontal tissues. For those with PLS, rapid periodontal breakdown could result in loss of some of the dentition.[1] However, the literature shows that mechanical therapy combined with an antibiotic regimen can successfully control the periodontal signs of PLS and result in the maintenance of a healthy dentition.[11,14,17,20] Furthermore, implant therapy has proved to be successful in these patients.[40]

Therefore, PLS patients with mild skeletal Class III relationship could benefit from early facemask therapy. Implant anchorage system can be incorporated to reinforce the orthopedic correction effect and to enhance the prognosis of the controlled dentition.

An onplant in the palate has been reported to aid in securing anchorage for facemask therapy.[41,42] A modified transpalatal arch can be attached to the onplant with extended hooks in the buccal vestibule to create a proper point of force application from the facemask. However, because of the severity of the skeletal discrepancies in our sample and the strict regimen required to maintain a healthy dentition, orthognathic surgery might be a treatment alternative for these patients after completion of facial growth.

Our final sample comprised 8 subjects. The limited sample size was the result of the extremely low prevalence of PLS and our strict inclusion and exclusion criteria.[33] These criteria resulted in a minimized bias where absence of posterior stop may lead to an anterior rotation of the mandible and a decreased facial height, which can produce a false Class III diagnosis. Although sample size was small, subjects in the present study were recruited from an initial sample of 47 patients with PLS, showing clinically varying degrees of Class III dentofacial pattern. Other limitations of our sample were the wide age range and the presence of siblings. However, the dentofacial pattern of their parents did not reflect such a relationship. Furthermore, the cephalometric findings of these siblings blended homogenously with the rest of the group.

This study can serve as a guide for future studies. A larger representative sample is essential to confirm our findings and to justify an evidence-based management protocol.

CONCLUSIONS

Patients with PLS generally have the following features:

1. Class III skeletal relationship, mainly due to a retrognathic and hypoplastic maxilla.
2. Decreased lower facial height, mainly because of posterior (clockwise) inclination of the maxilla.
3. Retroclination of the mandibular incisors as a compensation for maxillary retrognathism.
4. Upper lip retrusion.

REFERENCES

1. Hart TC, Shapira L. Papillon-Lefèvre syndrome. Periodontol 2000 1994;6:88-100.
2. Ullbro C, Crossner CG, Nederfors T, Alfadley A, Thestrup-Pedersen K. Dermatologic and oral findings in a cohort of 47 patients with Papillon-Lefèvre syndrome. J Am Acad Dermatol 2003;48:345-51.
3. Rudiger S, Berglundh T. Root resorption and signs of repair in Papillon-Lefèvre syndrome. A case study. Acta Odontol Scand 1999;57:221-4.
4. Hart TC, Hart PS, Bowden DW, Michalec MD, Callison SA, Walker SJ, et al. Mutations of the cathepsin C gene are responsible for Papillon-Lefèvre syndrome. J Med Genet 1999; 36:881-7.
5. Toomes C, James J, Wood AJ, Wu CL, McCormick D, Lench N, et al. Loss-of-function mutations in the cathepsin C gene result in periodontal disease and palmoplantar keratosis. Nat Genet 1999; 23:421-4.
6. Ullbro C, El-Samadi S, Boumah C, Al-Yousef N, Wakil S, Twetman S, et al. Phenotypic variation and allelic heterogeneity in young patients with Papillon-Lefèvre syndrome. Acta Derm Venereol 2006;86:3-7.
7. de Haar SF, Tigchelaar-Gutter W, Everts V, Beertsen W. Structure of the periodontium in cathepsin C-deficient mice. Eur J Oral Sci 2006;114:171-3.
8. Lefevre C, Blanchet-Bardon C, Jobard F, Bouadjar B, Stalder JF, Cure S, et al. Novel point mutations, deletions, and polymorphisms in the cathepsin C gene in nine families from Europe and North Africa with Papillon-Lefèvre syndrome. J Invest Dermatol 2001;117:1657-61.
9. Nakano A, Nomura K, Nakano H, Ono Y, LaForgia S, Pulkkinen L, et al. Papillon-Lefèvre syndrome: mutations and polymorphisms in the cathepsin C gene. J Invest Dermatol 2001;116:339-43.
10. Zhang Y, Lundgren T, Renvert S, Tatakis DN, Firatli E, Uygur C, et al. Evidence of a founder effect for four cathepsin C gene mutations in Papillon-Lefèvre syndrome patients. J Med Genet 2001;38:96-101.
11. Wiebe CB, Hakkinen L, Putnins EE, Walsh P, Larjava HS. Successful periodontal maintenance of a case with Papillon-Lefèvre syndrome: 12-year follow-up and review of the literature. J Periodontol 2001;72:824-30.
12. De Vree H, Steenackers K, De Boever JA. Periodontal treatment of rapid progressive periodontitis in 2 siblings with Papillon-Lefèvre syndrome: 15-year follow-up. J Clin Periodontol 2000; 27:354-60.
13. Eickholz P, Kugel B, Pohl S, Naher H, Staehle HJ. Combined mechanical and antibiotic periodontal therapy in a case of Papillon-Lefèvre syndrome. J Periodontol 2001;72:542-9.

14. Pacheco JJ, Coelho C, Salazar F, Contreras A, Slots J, Velazco CH. Treatment of Papillon-Lefèvre syndrome periodontitis. J Clin Periodontol 2002;29:370-4.
15. Ullbro C, Brown A, Twetman S. Preventive periodontal regimen in Papillon-Lefèvre syndrome. Pediatr Dent 2005;27:226-32.
16. Tinanoff N, Tanzer JM, Kornman KS, Maderazo EG. Treatment of the periodontal component of Papillon-Lefèvre syndrome. J Clin Periodontol 1986;13:6-10.
17. Preus H, Gjermo P. Clinical management of prepubertal periodontitis in 2 siblings with Papillon-Lefèvre syndrome. J Clin Periodontol 1987;14:156-60.
18. Robertson KL, Drucker DB, James J, Blinkhorn AS, Hamlet S, Bird PS. A microbiological study of Papillon-Lefèvre syndrome in two patients. J Clin Pathol 2001;54:371-6.
19. Hart TC, Bowden DW, Ghaffar KA, Wang W, Cutler CW, Cebeci I, et al. Sublocalization of the Papillon-Lefèvre syndrome locus on 11q14-q21. Am J Med Genet 1998;79:134-9.
20. Kim JB, Morita M, Kusumoto M, Watanabe T, Takagi S, Nishijima K. Preservation of permanent teeth in a patient with Papillon-Lefèvre syndrome by professional tooth-cleaning. ASDC J Dent Child 1997;64:222-6.
21. Lux CJ, Kugel B, Komposch G, Pohl S, Eickholz P. Orthodontic treatment in a patient with Papillon-Lefèvre syndrome. J Periodontol 2005;76:642-50.
22. Dahlberg G. Statistical methods for medical and biological students. New York: Interscience Publications; 1940.
23. Hashim H. Soft tissue relation in a sample of adult Saudi males. Egypt Dent J 2002;48:523-9.
24. Alnamankani EA. The comparative investigation of the components of Class III malocclusion in a sample of adult Saudi patients [thesis]. Riyadh, Saudi Arabia: King Saud University; 2004.
25. Korbmacher H, Moeller HC, Klocke A, Limbrock J, Kahl-Nieke B. Cephalometric evaluation of children with Down syndrome after early intervention with the stimulating plate. Spec Care Dentist 2005;25:253-9.
26. De Coster P, De Pauw G, Martens L, De Paepe A. Craniofacial structure in Marfan syndrome: a cephalometric study. Am J Med Genet A 2004;131:240-8.
27. Kreiborg S, Aduss H, Cohen MM Jr. Cephalometric study of the Apert syndrome in adolescence and adulthood. J Craniofac Genet Dev Biol 1999;19:1-11.
28. Laitinen SH, Ranta RE. Cephalometric measurements in patients with Pierre Robin syndrome and isolated cleft palate. Scand J Plast Reconstr Surg Hand Surg 1992;26:177-83.
29. Tarjan I, Balaton G, Balaton P, Vajo Z. The role of dental evaluation and cephalometric analysis in the diagnosis of Williams-Beuren syndrome. Wien Klin Wochenschr 2005;117:226-8.
30. Kane AA, Liao YF, Lo LJ, Huang CS, Huang LM, Chen YR, et al. A cephalometric study of facial growth in van der Woude syndrome. Cleft Palate Craniofac J 2002;39:219-25.
31. Hennekam RC, Van den Boogaard MJ, Van Doorne JM. A cephalometric study in Rubinstein-Taybi syndrome. J Craniofac Genet Dev Biol 1991;11:33-40.
32. Schaedel R, Poole AE, Cassidy SB. Cephalometric analysis of the Prader-Willi syndrome. Am J Med Genet 1990;36:484-7.
33. Griffiths WA, Leigh IM. Disorders of kertinization. In: Champion RH, Burton JL, Burns TA, Breathnach SM, editors. Rook/Wilkinson/Ebling: textbook of dermatology. Hoboken, NJ: Wiley; 1998. p. 1483-588.
34. Hurmerinta K, Pirinen S, Kovero O, Kivitie-Kallio S. Craniofacial features in Cohen syndrome: an anthropometric and cephalometric analysis of 14 patients. Clin Genet 2002;62:157-64.
35. Murdoch-Kinch CA, Bixler D, Ward RE. Cephalometric analysis of families with dominantly inherited Crouzon syndrome: an aid to diagnosis in family studies. Am J Med Genet 1998;77:405-11.
36. Naidoo S, Harris A, Swanevelder S, Lombard C. Foetal alcohol syndrome: a cephalometric analysis of patients and controls. Eur J Orthod 2006;28:254-61.
37. Horswell BB, Holmes AD, Levant BA, Barnett JS. Cephalometric and anthropomorphic observations of Binder's syndrome: a study of 19 patients. Plast Reconstr Surg 1988;81:325-35.
38. Ngan PW, Hagg U, Yiu C, Wei SH. Treatment response and long-term dentofacial adaptations to maxillary expansion and protraction. Semin Orthod 1997;3:255-64.
39. Franchi L, Baccetti T, McNamara JA. Postpubertal assessment of treatment timing for maxillary expansion and protraction therapy followed by fixed appliances. Am J Orthod Dentofacial Orthop 2004;126:555-68.
40. Ullbro C, Crossner CG, Lundgren T, Stalblad PA, Renvert S. Osseointegrated implants in a patient with Papillon-Lefèvre syndrome. A 4 1/2-year follow up. J Clin Periodontol 2000;27:951-4.
41. Block MS, Hoffman DR. A new device for absolute anchorage for orthodontics. Am J Orthod Dentofacial Orthop 1995;107:251-8.
42. Hong H, Ngan P, Han G, Qi LG, Wei SH. Use of onplants as stable anchorage for facemask treatment: a case report. Angle Orthod 2005;75:453-60.