Panoramic Radiographic Representation of Progressive Periodontal Destruction in a Family with Six Affected Papillon-Lefèvre Siblings.

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The panoramic radiographs of six Papillon-Lefèvre affected siblings from one family are evaluated and compared. These six affected siblings range in age from seven to twenty-four years of age. Tooth loss and periodontal disease progression are radiographically documented as these affected siblings age and eventually become endentulous with evident ridge resorption

Keywords: *Papillon-Lefèvre, hyperkeratosis ,palmo-plantar, edentulous*
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INTRODUCTION

Papillon-Lefèvre syndrome (PLS) is a rare autosomal recessive condition noted for severely progressive periodontal disease and hyperkeratosis of the palms of the hands and the soles of the feet. The periodontal symptoms persist through both the primary and adult dentitions. It has a prevalence rate of 1-4 *per* million.[1,2] Over 200 cases have been reported in the literature since the initial report in 1924.[1,3] There does not appear to be any noticeable ethnic or gender predilection.[4,5] Consanguinity is prevalent among parents of PLS affected siblings in a significant number of cases.[4,6,7] Calcification of the dura has also been reported as a potential finding consistent with the syndrome.[2,8,9] PLS may manifest as early as two months of age with the appearance of hyperkeratotic lesions of the palms and soles. Usually, the palmo-plantar hyperkeratosis appears almost simultaneous with the periodontal lesions between the ages of 1 to 4 years.[1] Premature exfoliation of the primary teeth results in a disease-free oral environment until the pattern repeats itself with the eruption of the permanent dentition. The patient is usually totally edentulous by late teens despite rigorous periodontal therapy.[4,10] Complete dentures are usually well tolerated.[1,4]

Within the progression of oral disease, the patient typically experiences tooth looseness, hypermobility, drifting, migration and exfoliation of the teeth without evident signs of root resorption. Furthermore, tooth mobility leads to pain on chewing. The radiographic features include interproximal angular defects, furcation radiolucencies and severe loss of alveolar bone around the teeth leading to a "floating in air" radiographic appearance.[4,7] However, others have found variable penetrance and less severe periodontal disease.[10–12] Diagnosis is determined primarily with regard to PLS findings consistent with previous reported cases and secondarily with regard to genetic markers.[13–15]

PLS is associated with various host responses such as neutrophil chemotactic, bacteriocidal, and phagocytotic dysfunction, depression of helper to suppressor T-cell ratio, deficient monocytic function and elevation of serum immunoglobulins.[6,16-20] Such pathogenic micro-organisms as *Porphyromonas gingivalis, Capnocytophaga gingivalis, Aggregatibacter actinomycetemcomitans, Peptostreptococcus micros, Treponema denticola, Prevotella intermedia, Tannerella forsythus, Fusobacterium nucleatum*, and spirochetes have been implicated as the periodontal pathogens associated with this syndrome.[21-24]

The purpose of this paper is to demonstrate the radiographic progression of PLS utilizing panoramic radiographs taken at the same point in time on a family (Family #2 in Ghaffar *et al*., 1999) of six affected siblings at 7, 11, 14, 15, 19 and 24 years of age.[6]

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CASE REPORTS

The family pedigree is demonstrated in Figure 1. The three oldest siblings did not demonstrate periodontal disease or hyperkeratotic lesions of the soles of the feet and the palms of the hand. The six youngest siblings, however, did demonstrate the characteristic findings of Papillon-Lefèvre syndrome such as severe periodontal disease and hyperkeratotic lesions of the palms of the hands and soles of the feet.

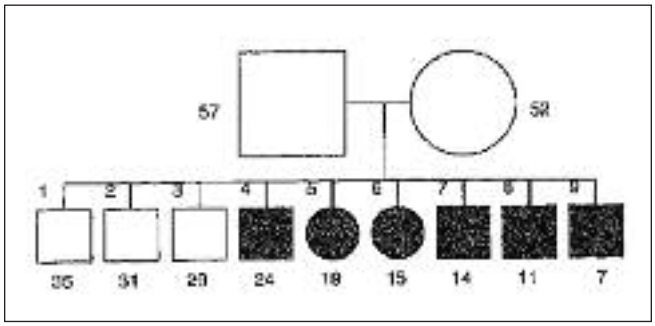

Figure 1. Family Pedigree: Circle – female; Square – male; Unfilled – Either parent or unaffected sibling; Filled – affected sibling (with permission from Elsevier Ghaffar et al 1999)

Case 1

The first case is the seven year-old male affected sibling. The most striking feature of the panoramic radiograph (Figure 2A) is the total absence of primary teeth. Clinically, this 7 year old child presents with all four fully erupted first molars and several erupted or partially erupted incisors, the maxillary left central and the mandibular central and lateral incisors. There is no significant evidence of periodontal bone loss within the radiograph. Many un-erupted teeth are present including the maxillary second molars, first and second bicuspids, canines, laterals and the right central incisor and the mandibular second molars, first and second bicuspids and the canines. The maxillary bicuspids appear to be rotated 90 degrees. The clinical picture (Figure 2B) reveals moderate supragingival plaque on the mandibular incisors and mild gingival erythema.

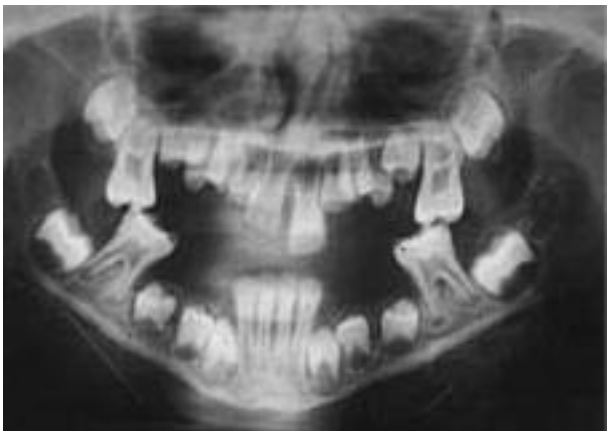

Figure 2 A: Panoramic radiograph of 7 year old affected sibling, Case #1

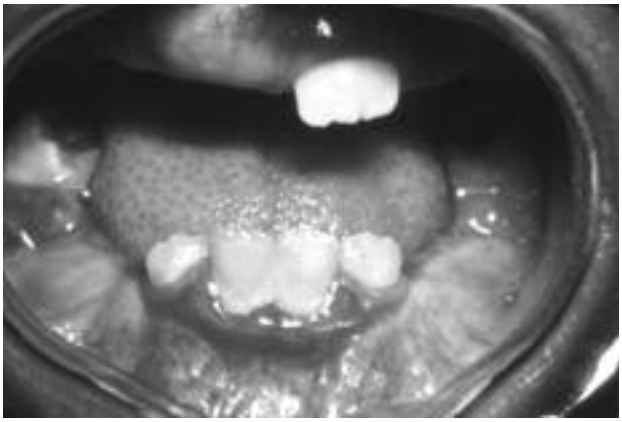

Figure 2 B: Clinical slide of 7 year-old affected sibling, Case #1

Case 2

The second case is the eleven year-old male affected sibling. The panoramic radiograph (Figure 3) reveals severe generalized bone loss among the erupted teeth. Furcation involvement is noted for mandibular left second molar and both maxillary second molars. Furthermore, several teeth demonstrate drifting and super-eruption. The erupted teeth include the maxillary second molars, first and second bicuspids, canines, lateral and central incisors and the mandibular second molars, first and second bicuspids, canines, and lateral incisors. All the first molars and mandibular central incisors are missing. The third molars are all present and unerupted

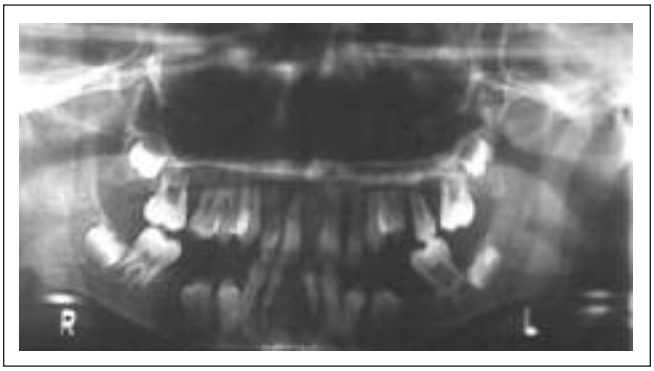

Figure 3: Panoramic radiograph of 11 year old affected sibling, Case #2

Case 3

The third case is a 14 year-old male affected sibling. The panoramic radiograph (Figure 4A) reveals that the maxillary second molars and second bicuspids are present. Also, the maxillary right first bicuspid and canine are present. The mandibular second molars and first bicuspids are present as are the mandibular right second bicuspid and canine. The mandibular third molars appear to be partially erupted and the maxillary third molars appear to be un-erupted. Severe bone loss of all the erupted teeth is noted. The mandibular

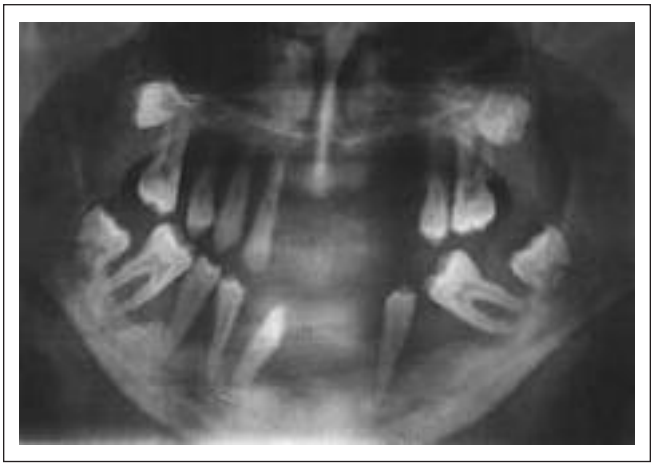

Figure 4A: Panoramic radiograph of 14 year old affected sibling, Case #3

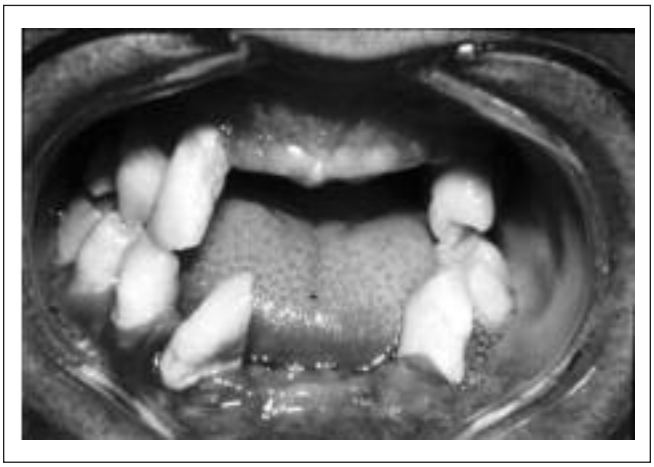

Figure 4B: Clinical figure of 14 year-old affected sibling, Case #3

second molars demonstrate the characteristic "floating in air" appearance. The third molars are all present and unerupted. The clinical slide (Figure 4B) reveals heavy deposits of supragingival plaque and staining, along with severe generalized gingival erythema.

Case 4

The forth case is a 15 year-old female sibling. The panoramic radiograph (Figure 5) reveals that only the third molars are erupted and present. The mandibular third molars demonstrate substantial horizontal bone loss and the maxillary third molars demonstrate moderate bone loss. Furthermore, extensive ridge resorption is noted for both the maxilla and mandible.

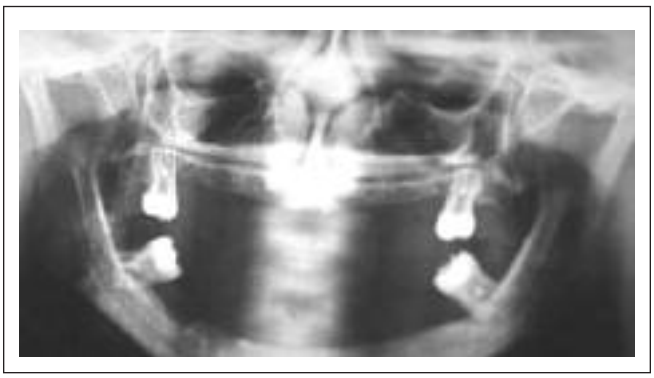

Figure 5. Panoramic radiograph of 15 year old affected sibling, Case #4

Case 5

The fifth case is a 19 year-old female affected sibling. The panoramic radiograph (Figure 6) reveals that the only tooth present is the maxillary right third molar. Retention wire clasps are evident in the radiograph representing acrylic removable partial treatment dentures. Radiographically, the maxillary right third molar is noted for severe generalized horizontal bone loss with a suspected furcation involvement. Severe resorption of both the maxilla and the mandible is evident. .

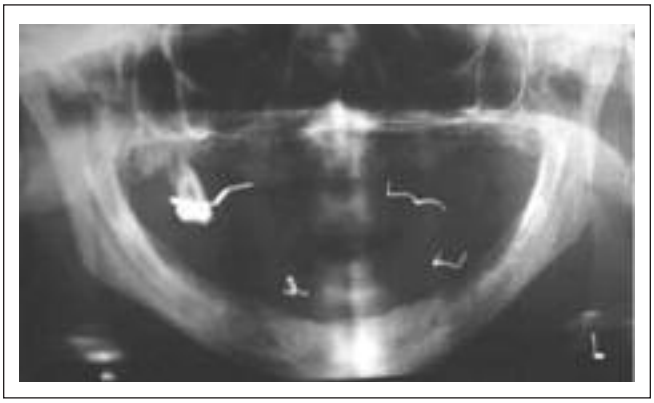

Figure 6. Panoramic radiograph of 19 year old affected sibling, Case #5

Case 6

The sixth case is a 24 year-old male affected sibling. The panoramic radiograph (Figure 7) reveals that this patient is completely edentulous, with severely resorbed maxilla and mandible.

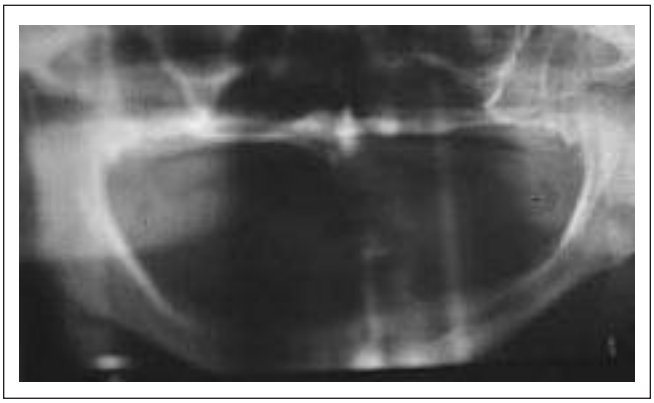

Figure 7. Panoramic radiograph of 24 year old affected sibling, Case #6

DISCUSSION

The radiographic progression of severely progressive periodontal disease is evident in viewing the series of panoramic

radiographs of the six affected PLS siblings. The panoramic of the seven-year-old demonstrates that all the adult dentition is visible with the exception of the third molars. The four first molars, the maxillary left central and the mandibular incisors are erupted. It is reasonable to assume that the rotation of the maxillary premolars may have been influenced by the premature loss of the primary dentition. The panoramic radiograph of the eleven year old demonstrates that all the first molars are missing along with the mandibular central incisors. Presumably, these teeth were the first teeth to erupt and the first to exfoliate. The panoramic of the fourteen year old demonstrates severe bone loss of the remaining dentition (with the exception of the third molars which are not yet erupted). Only the second molars and two canines and six bicuspids are still present. The panoramic of the fifteen year old patient demonstrates that only the third molars remain. The panoramic of the nineteen year old demonstrates only the presence of one remaining tooth, the maxillary right third molar that appears to demonstrate significant bone loss. Also, the mandible particularly demonstrates significant bone resorption. The panoramic radiograph of the twenty four year old demonstrates complete edentulism along with significant alveolar ridge resorption.

The affected siblings in the family reported upon did not have ready access to dental care. Their care was limited mainly to extraction and prosthetics. Continued periodontal care was not available. As with most reported PLS cases, the affected siblings within this family suffered from severe periodontal disease and the early complete loss of dentitions. Figure 1 demonstrates the family tree. The parents are noted to be unaffected by PLS. The three eldest siblings were all unaffected by PLS. The six youngest siblings are all affected with PLS.

PLS affected siblings within this family and PLS affected siblings from three other families were evaluated for cellular immunity with regard to phagocytosis, intracellular killing, and opsonization.[6] It was determined that the PLS affected siblings within this family had diminished immune neutrophil phagocytotic and intracellular killing attributes but not with regard to opsinization compared to age- and gender-matched sibling controls and unrelated age- and gender-matched controls. Categorically, these PLS affected siblings had diminished immune competence capacity with regard to periodontal infection. This diminished immune competence was demonstrated both with regard to laboratory studies and in the extreme early progression of periodontal disease as demonstrated by the series of panoramic radiographs.

Several authors have reported that stringent plaque control and professional non-surgical periodontal therapy may be associated with some therapeutic successes.[3,23,25-27] As delineated above in Table I, several case reports and studies have noted reasonably successful periodontal therapy of PLS patients.[4,21-28] Many of these cases utilized a therapeutic philosophy of antibiotic therapy particularly after the complete loss of the primary dentition previous to the eruption of the adult dentition. (The complete loss of the primary dentition is evident within the panoramic radiograph of the seven year-old male affected sibling.) However, therapeutic failures were noted as utilizing the same or similar therapeutic concepts and modalities.[4,21] Lux and co-workers also utilized orthodontic therapy. With the complete loss of the primary dentition, there is little guidance with regard to the eruption pattern of the adult dentition in PLS patients. Perhaps the adjunctive orthodontic therapy utilized by Lux and co-workers contributed to the successful therapy. As these cases were not controlled nor blinded and in that PLS appears to have variable degrees of penetrance, it is impossible to determine whether or not the successful or unsuccessful resolution of periodontitis in such cases was determinate upon patient compliance, therapeutic modalities, or host resistance or any combination of these and other factors.[4,21-26]

Table I - PLS Treatment Case Reports

Author(s)	Success	Failure	Follow-up period
Toygur *et al* (2007)	1	-	13 years
Ahuja *et al* (2005)	1	-	1 year
Lux *et al* (2005)	1	-	79 months
Lundgren & Renvert (2004)	2	3	3 years
Pacheo *et al* (2002)	1	-	16 months
Wiebe *et al* (2001)	1	_	12 years
De Vree *et al* (2000)	1	1	15 years
Tinanoff *et al* (1995)	1	-	15 years
Preus (1988)	2	-	15 months

Within the last decade, the importance of genetics with regard to PLS has been evaluated. In fact, genetic material from Family #2 of the 6- Ghaffar *et al* [6] study was included within the Hart et al.,[15] study utilized to explore and define some of the genetic issues with regard to PLS. Specifically, a gene abnormality found on chromosome 11q14 has been implicated. Genomics has determined the involvement of the protein cathepsin C. Even though the pathophysiology of PLS is presently unresolved, it has been hypothesized that the absence of functional cathepsin C is important with regard to the structural integrity of protective barriers formed by gingival, skin, and immune cells. Therefore, the immune response is deficient particularly within gingival and cutaneous tissues.[13-15] The fact that PLS results in severe intractable (or at least very difficult to successfully treat) periodontal disease and is an autosomal recessive condition has very special considerations, particularly for the family presented. As the sequential panoramic radiographs of the affected siblings noted, the condition in this family manifested as a severe periodontal infection with eventual complete loss of dentition appearing to be the end result. There is obvious concern with regard to passing on this condition to future children of both the affected and unaffected siblings and their offspring. The parents were unaffected but nevertheless PLS carriers which demonstrates the autosomal recessive nature of the condition. Possibly, the parents through genetic counseling may have been persuaded to seek other marriage partners. Certainly, the affected and unaffected siblings may benefit from genetic family counseling The parents could have had an opportunity to limit

the births of children with the genotype that expresses PLS. Certainly, the affected and unaffected siblings may wish to consider family counseling, fetal DNA testing and other alternatives with regard to passing on a genetic predisposition for PLS.[13-15]

Presently new frontiers have been entered regarding genetic and molecular testing technology. Amniocentesis and chorionic villus sampling have the potential to allow for identification of many genetic syndromes. Comparative genomic hybridization utilizing microarrays have the potential to detect these severe syndromes. In patients with known propensities such as the siblings of the PLS family evaluated currently and their offspring, standard genetic analysis would probably be sufficient. These new technologies can target devastating genetic syndromes such as Tay-Sachs and also lesser but certainly relatively severe syndromes such as PLS. This technology has the ability to decrease the rate of problematic births regarding such syndromes as PLS.[13-15] Potential actions such as abortion, family counseling, genetic testing, amniocentesis and chorionic villus sampling are all possible presently. Because of recent advances in science, ethical issues are brought forth.

In conclusion, the panoramic radiographs presented within this report document the continued severe periodontal progression of Papillon-Lefèvre syndrome in one particular family. These radiographic data demonstrate a cross-sectional vision of the progression of the condition over time.

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