J Clin Periodontol 2004; 31: 933–938 doi: 10.1111/j.1600-051X.2004.00591.x
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Journal of Clinical Periodontology

Periodontal treatment of patients with Papillon–Lefèvre syndrome: a 3-year follow-up

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Lundgren T, Renvert S: Periodontal treatment of patients with Papillon–Lefèvre syndrome: a 3-year follow-up. J Clin Periodontol 2004; 31: 933–938. doi: 10.1111/j.1600-051X. 2004.00591.x. © Blackwell Munksgaard, 2004.

Abstract

Background/aim: Conventional mechanical periodontal treatment of Papillon–Lefèvre syndrome (PLS) has often been reported to fail. This study describes the outcome of a non-surgical periodontal therapy including antimicrobial treatment of nine patients diagnosed with PLS. The patients originate from a total of 15 children and adolescents with PLS for which clinical characteristics are presented.

Methods: Clinical examination including conventional periodontal measurements. Initial treatment including oral hygiene instruction, scaling and root planing and systemic amoxicillin–metronidazole therapy for 6 weeks. After that the patients were enrolled in a 3-month recall maintenance program. In addition to this mechanical supportive maintenance treatment, tetracycline was prescribed and used continuously for 1.5 years.

Results/Conclusion: On five patients who were showing acceptable standard of oral hygiene and also compliance with the antibiotic medication, development of periodontitis on erupting teeth was prevented and disease activity on the previously periodontally involved teeth controlled during a 3-year period. Poor results of treatment were observed for three patients, all siblings. These patients failed to comply with the medication and also failed to improve their oral hygiene.

Key words: Papillon–Lefèvre syndrome; periodontitis; treatment

Accepted for publication 2 February 2004

Papillon–Lefèvre syndrome (PLS) is characterized by hyperkeratosis of hands and feet and by a generalized aggressive periodontitis in both the primary and the permanent dentition (Papillon & Lefèvre 1924). The recently identified genetic defect in PLS has been mapped to chromosome 11q14–q21, which involves mutations of cathepsin C (Hart et al. 1999, Toomes et al. 1999). Studies in PLS patients have shown more than 90% reduction in cathepsin C activity (Toomes et al. 1999, Hart et al. 2000). The main function of cathepsin C is thought to be protein degradation and proenzyme activation (Rao et al. 1997). The lack of functional cathepsin C in PLS may be associated with a reduced host response against bacteria in dental plaque (Oguzkurt et al. 1996). Despite these advances in characterizing the genetic basis of the syndrome, the pathogenic mechanisms leading to the periodontal involvement remain elusive.

An impaired chemotactic and phagocytic function of polymorphonuclear leukocytes (PMNs) has been described in many reports (Borroni et al. 1985, Bimstein et al. 1990, D'Angelo et al. 1992, Brown et al. 1993, Bullon et al. 1993, Tinanoff et al. 1995, Firatli et al. 1996, Boutsi et al. 1997, Ghaffer et al. 1999, Liu et al. 2000). In contrast to the above studies, Lyberg (1982) and Schroeder et al. (1983), however, reported normal PMN chemotaxis. Few reports have addressed lymphocyte function in PLS. Some reports document decreased proportions of certain lymphocyte subpopulations (Çelenligil et al. 1992, D'Angelo et al. 1992, Gongora et al. 1994), while other reports have failed to find any change in the peripheral lymphocyte populations (Levo et al. 1980, Firatli et al. 1996). Thus, the available reports on immunological alterations in PLS patients do not provide any consistent findings. This has left the question of whether immunologic functions are impaired in PLS unanswered.

It has been suggested that the development of periodontal disease in PLS patients might be associated with a specific profile of suspected subgingival pathogens coupled with some still unknown nature of altered and reduced immune defence. In a number of case reports, *Actinobacillus actinomycetemcomitans* has been observed in subgingival plaque samples from periodontal pockets in cases with PLS (Van Dyke

et al. 1984, Preus 1988, Vrahopoulos et al. 1988, Bimstein et al. 1990, Eronat et al. 1993, Ishikawa et al. 1994, Kressin et al. 1995, Tinanoff et al. 1995, Kleinfelder et al. 1996, Boutsi et al. 1997, Rüdiger et al. 1999, De Vree et al. 2000, Eickholz et al. 2001, Wiebe et al. 2001, Pacheco et al. 2002). Other putative periopathogens including *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, *Bacteroides forsythus*, *Treponema denticola* and *Prevotella intermedia* have also been implicated to play a role in PLS periodontal pathogenesis (Clerehugh et al. 1996, Velazco et al. 1999). The subgingival microbial profile for patients of the present study was reported previously (Lundgren et al. 1998). Our analyses failed to demonstrate a PLS-specific profile of the subgingival infection, as the bacterial composition of the sampled sites closely resembled that characterizing deep pockets in adult periodontitis patients.

Early case reports on periodontal treatment in PLS patients describe unsuccessful outcome and tooth loss leading to edentulism as an unavoidable part of this syndrome (Gorlin et al. 1964, Haim & Munk 1965, Krebs 1978). Treatment with oral hygiene instructions and scaling and root planing has been reported unsuccessful (Hathway 1982, Bimstein et al. 1990, Hattab et al. 1995). Non-surgical treatment combined with use of systemic antibiotics (Rateitschak-Plüss & Schroeder 1984, Glenwright & Rock 1990, Bullon et al. 1993, De Vree et al. 2000) and additional periodontal surgery (Van Dyke et al. 1984, Bullon et al. 1993) has also been reported to fail.

One proposed mode of periodontal treatment in PLS has been to extract all primary teeth in order to decrease the risk of transferring the microbiota from infected sites in the primary dentition to the permanent dentition. Baer & McDonald (1981) recommended extractions of all deciduous teeth by 3 years of age followed by a 3-month edentulous period prior to insertion of full dentures. Systemic tetracycline was recommended at the time of denture insertion and as the permanent teeth were erupting. Variants of this protocol have been advocated by Preus & Gjermo (1987) and Tinanoff et al. (1986, 1995).

Some recent reports describe a positive response to periodontal treatment in PLS. The non-surgical periodontal treatment of these patients was often combined with extractions of severely affected teeth, use of systemic antibiotics and supportive maintenance care. Erupting teeth and even some of the teeth showing periodontal disease were successfully treated and kept healthy for an extended length of time (Preus & Gjermo 1987, Ishikawa et al. 1994, Boutsi et al. 1997, Rüdiger et al. 1999, De Vree et al. 2000, Pacheco et al. 2002). Although these reports are limited to descriptions of successful outcome in few patients only, they suggest that there might be a possibility to halt the periodontal disease process if one uses a combined, intensive mechanical and antimicrobial treatment approach in PLS patients. The present report describes the outcome following treatment of nine patients using such an approach, including a 3-year follow-up.

Material and Methods

Subjects

The nine cases described in this report originate from a total of 15 children and adolescents, 6–18 years of age, diagnosed with PLS in accordance with the criteria by Papillon & Lefèvre (1924) and referred to the periodontal clinic at King Faisal Specialist Hospital & Research Center in Riyadh, Saudi Arabia.

Characteristics for these 15 patients are presented in Table 1. Sibling groups accounted for 14 of the 15 patients. Consanguinity of parents could be confirmed for all 15 patients. Calcifications of falx cerebri were radiographically found for two patients. Parents of four patients reported a history of susceptibility to milder infections like colds, ear and skin infections of their children. Six patients were on retinoid medication. Parents of all patients reported that the patients had lost all their primary teeth as a result of periodontitis. Four patients had received periodontal treatment including extractions of severely involved teeth, repeated oral hygiene instructions, chlorhexidine rinsing, scaling and root planing, periodontal surgery and intermittent prescription of antibiotics.

All patients except one demonstrated poor oral hygiene. Typically, the gingiva was red, swollen and bled easily on probing. Most teeth demonstrated increased probing depth. Sulcular purulent exudate was a common finding from teeth with deep lesions. Four patients had severe halitosis. Six of the 15 patients demonstrated severe periodontitis deemed untreatable on all erupted permanent teeth resulting in extractions after the initial examination (numbers 10–15). These patients were provided with full dentures. Among the remaining nine patients, extractions of teeth considered untreatable were also performed, leaving a variable number of permanent teeth to be treated (Table 1).

Table 1. Age, gender (M, male; F, female), consanguinity of parents, calcification of falx cerebri, susceptibility to infection, retinoid medication, previous periodontal treatment, number of teeth and number of extractions at the initial examination

Patient	Age	Gender	Cons.	Calcif.	Sus. to inf.	Retinoid med.	Treatment	No. of teeth	No. of teeth extracted*
1†	10	F	+	–	–	+	–	6	2
2†	8	F	+	–	–	–	–	6	4
3†	14	M	+	–	+	–	+	18	8
4‡	9	M	+	–	+	+	+	9	6
5‡	11	F	+	–	–	–	+	18	4
6§	11	M	+	–	–	–	–	9	2
7¶	6	F	+	–	–	+	–	2	0
8¶	11	M	+	–	–	+	–	3	1
9¶	8	F	+	–	–	+	–	7	4
10	14	F	+	+	+	+	+	5	5
11¶	14	F	+	+	+	–	–	16	16
12§	14	F	+	–	–	–	–	15	15
13**	14	F	+	–	–	–	–	10	10
14**	17	M	+	–	–	–	–	2	2
15**	18	M	+	–	–	–	–	4	4

*Teeth deemed untreatable at initial extraction.
†Patients 1–3 are siblings.
‡Patients 4–5 are siblings.
§Patients 6 and 12 are siblings.
¶Patients 7–9 and 11 are siblings.
**Patients 13–15 are siblings.

Treatment

The treatment protocol was designed together with the physicians responsible for the patients' medical care.

In a previous, retrospective study of our PLS patients, we did not observe any positive effects of retinoid medication on periodontal health (Lundgren et al. 1996). Therefore, after consulting the patients' dermatologists, it was decided to discontinue the retinoid medication, considering the relatively positive effects of local treatment of the skin lesions, and the potential adverse effects of the retinoid drugs.

Periodontal treatment was initiated with an intensive non-surgical treatment in several visits during 6 weeks, including oral hygiene instruction, professional polishing, scaling and root planing and instructions to rinse with chlorhexidine (0.2%) for 1 min, twice daily. During this entire 6-week treatment phase, the patients were prescribed to use amoxicillin (250 mg twice/day) and metronidazole (250–500 mg three times/day). Compliance with the antibiotic regime was asked and recorded at each treatment visit.

After the initial 6-week treatment period, all patients were scheduled for maintenance care every 3 months. At the maintenance visits, the oral hygiene level was categorized from an overall evaluation by the therapist (excellent, fair, good or poor). Oral hygiene was reinforced and the teeth were polished using rubber cup and sodium fluoride polishing paste. Supra- and subgingival scaling was performed as needed. In addition to this mechanical maintenance treatment, tetracycline (250 mg/day) was prescribed and used continuously for 1.5 years. Compliance with this antibiotic medication was inquired and recorded at each maintenance visit.

Results

The outcome of treatment for teeth considered treatable after initial examination is presented in Table 2. In four patients (numbers 1–4), all these teeth had probing depth $\leqslant 3$ mm at the 3-year follow-up. In two patients (numbers 5 and 6), a few teeth had residual probing depth $\geqslant 4$ mm. In three patients (numbers 7–9), treatment had been unsuccessful leading to extractions.

The treatment results for teeth erupting during the 3-year observation period are shown in Table 3. In five patients (numbers 1, 2 and 4–6), no lesion $\geqslant 6$ mm had developed at these teeth. In three patients (numbers 7–9), periodontal disease developed following eruption of several teeth resulting in extractions.

An overall evaluation of treatment outcome for the nine patients is presented in Table 4. Results of treatment have been classified as excellent to poor based upon the findings presented in Tables 2 and 3. The degree of compliance with the antibiotic treatments and the predominant level of oral hygiene during the 3-year observation period for

Table 2. Treatment outcome for teeth present at initial examination

		No. of teeth with probing depth						
		$\leqslant 3$ mm		4–5 mm		$\geqslant 6$ mm		
Patient	No. of teeth*	initial	3 years	initial	3 years	initial	3 years	No. of teeth extracted
1	4	2	4	0	0	2	0	0
2	2	0	2	2	0	0	0	0
3	10	0	10	3	0	7	0	0
4	3	0	3	2	0	1	0	0
5	14	9	10	3	2	2	2	0
6	7	2	4	1	3	4	0	0
7	2	2	0	0	0	0	0	2
8	2	0	0	0	0	2	0	2
9	3	3	2	0	0	0	0	1

*After extraction of teeth considered untreatable.

Table 3. Treatment outcome for teeth erupting during the 3-year observation period

		No. of teeth with probing depth			
Patient	No. of teeth erupting	$\leqslant 3$ mm	4–5 mm	$\geqslant 6$ mm	No. of teeth extracted
1	11	11	0	0	0
2	16	12	4	0	0
3	0	0	0	0	0
4	10	10	0	0	0
5	6	5	1	0	0
6	5	2	3	0	0
7	8	4	0	0	4
8	13	2	2	7	2
9	10	4	0	0	6

Table 4. Overall evaluation of treatment outcome relative to compliance with the antibiotic medications, and to the maintenance of oral hygiene levels

Patient	Compliance with antibiotic medication*	Oral hygiene level†	Treatment outcome‡
1§	as prescribed	excellent	excellent
2§	as prescribed	excellent	excellent
3§	as prescribed	poor	excellent
4¶	as prescribed	good	excellent
5¶	as prescribed	fair	good
6	irregular	poor	fair
7**	not compliant	fair	poor
8**	not compliant	poor	poor
9**	not compliant	poor	Poor

*Based upon overall evaluation of recordings made during the initial 6 weeks of amoxicillin/metronidazole medication and the 1.5 years of tetracycline medication.
†Based upon the predominant ratings recorded at each of the 3-month maintenance visits during the entire observation period (subjective ratings by the therapist entered into patient records).
‡Based upon retention of teeth and absence of periodontal lesions during the 3-year observation period as described in Tables 2 and 3 (compare for details).
§Patients 1–3 are siblings.
¶Patients 4 and 5 are siblings.
**Patients 7–9 are siblings.

each patient are also shown in Table 4. It can be seen that treatment outcome classified as excellent or good was accomplished in five patients (numbers 1–5; two groups of siblings), all of whom had complied with the antibiotic medications. The oral hygiene levels in these patients varied from excellent to poor. Poor results of treatment were observed for three patients (numbers 7–9), all siblings. These patients failed to comply with the antibiotic medications and also failed to improve their oral hygiene.

Discussion

Haneke (1979) used the following three criteria to classify a case as PLS: (i) palmoplantar hyperkeratosis; (ii) loss of primary and permanent teeth; and (iii) autosomal recessive inheritance. The population prevalence of PLS is reported to be one case in 1–4 million people (Gorlin et al. 1964). With both parents as recessive carriers, there is a 25% chance of producing offspring with PLS (Hart & Shapira 1994). All 15 patients initially examined in our study had parent consanguinity, and sibling groups accounted for 14 of these 15 individuals. This is in concordance with reviews by Gorlin et al. (1964) and Haneke (1979) reporting that PLS displays a familiar aggregation.

Increased susceptibility to infections is reported for approximately 20% of PLS cases. Most of these reports describe susceptibility to furunculosis, pyogenic infections of the skin, bronchitis, tonsillitis and pneumonia (Gorlin et al. 1964, Haim & Munk 1965, Haneke et al. 1975, Bravo-Piris et al. 1983, Bergman & Friedman-Birnbaum 1988, Glenwright & Rock 1990, D'Angelo et al. 1992, Oguzkurt et al. 1996). Pyogenic liver abscesses for PLS patients has also been reported (Tosti et al. 1988, Khandpur & Reddy 2001, Almuneef et al. 2003). In our study, four of the patients reported a history of susceptibility to milder infections like colds, ear and skin infections.

Intracranial calcifications of falx cerebri in some PLS patients was reported by Brownstein & Skolnik (1972), El Darouti et al. (1988) and Kellum (1989). In the present study, calcifications of falx cerebri were radiographically found for two patients.

As mentioned before, in a previous, retrospective study of our PLS patients, we did not observe any positive effects of retinoid medication on periodontal health (Lundgren et al. 1996). Therefore, after consulting the patients' dermatologists, it was decided to discontinue this medication.

When our study started in 1994, there were only a few reports on successful outcome of treatment of periodontitis in PLS patients. Preus & Gjermo (1987) reported two siblings treated over a 4.5-year period. One of the patients, after having experienced 9 months of edentulousness, had four newly erupted teeth when treatment was started. These teeth and other teeth erupting during the study were kept healthy throughout the observation period. The other patient had deep periodontal pockets on six remaining teeth when treatment was started. Three of these teeth were extracted during the observation period but teeth with no involvement at the start of the study and teeth erupting during the period remained unaffected till the end of the study. Both patients were provided extensive periodontal treatment including tetracycline administration and supportive periodontal therapy. Use of tetracycline was intermittent for the first 2 years, but continuous during the following 2.5 years.

In all our patients, the primary teeth were lost before the start of the study. Most of the patients showed severe periodontitis. We decided to use an extensive treatment modality involving both mechanical and antimicrobial means of plaque and infection control. The choice of a combined amoxicillin and metronidazole therapy during the initial 6-week treatment phase was based on the documented effects of this combination on putative periodontal pathogens (van Winkelhoff 1989). Selection of tetracycline for our long-term use during maintenance was stimulated by the results of Preus & Gjermo (1987), coupled with the fact that tetracycline has been used over many years for long-term treatment of skin lesions, with a minimum of adverse effects (Del Rosso 2000).

In three of our patients, all siblings, the outcome of treatment was poor. These patients did not show compliance with the antibiotic medications. In addition, the oral hygiene level during the follow-up period was unsatisfactory. On the other hand, our results suggest that if the patients were compliant with the antibiotics regimen and if the overall oral hygiene level was adequate during the 3-year follow-up period, result of treatment was successful. This is in accordance with other authors reporting individual cases (Tinanoff et al. 1986, 1995, Preus & Gjermo 1987, Boutsi et al. 1997, Rüdiger et al. 1999, De Vree et al. 2000, Eickholz et al. 2001, Pacheco et al. 2002).

Although observations do not directly indicate that the level of oral hygiene stands out as the crucial factor for treatment outcome, it was our clinical impression that if patients were able to obtain an acceptable standard of oral hygiene, development of periodontitis on erupting teeth can be prevented and disease activity on the previously involved teeth controlled.

PLS patients are reported to complain about loose teeth, halitosis, swollen gums, food impaction and pain during chewing (Haneke 1979, Lu et al. 1987, Ghandour 1989). Multiple periodontal abscesses are common (Haneke 1979, Lu et al. 1987). Progressing periodontal disease leading to tooth loss is a major trauma in these children. Extensive and repeated orthodontic and prosthodontic treatment may become necessary to provide the children with a functional dentition during the growth period of their jaws. Edentulousness and placement of full dentures that need to be renewed at short intervals is an equally unappealing option. Against this background, an extensive and continuous mechanical and antimicrobial periodontal treatment like the one of the present report seems justified, in light of the fact that this treatment may lead to preservation of a periodontally healthy and functional dentition over several years in some patients.

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