Original Research Article

Long-term results after treatment of periodontitis in patients with Papillon–Lefèvre syndrome with or without antibiotics a comparative study

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Abstract

Aim: Evaluation of periodontal status in patients with Papillon–Lefèvre syndrome (PLS) observed for ≥5 years, Treatment of patients of PLS with SRP and maintenance for a period of ≥5 years, Comparing the effects of treatment of periodontitis in (PLS) patients with SRP (scaling and root planning) as a monotherapy with antibiotics as an adjunct.

Materials and methods: All subject showing signs and symptoms of PLS, were selected for this study comprising of both the sexes, visiting outpatient Department of Periodontology, Govt. Dental College and Hospital Srinagar. Eight patients (aged 5-12 years) from five families (three pairs of siblings) were included. Subjects were randomly distributed into two groups 4 patients each. Control group- Group A given SRP + Placebo and Treatment group- Group B given SRP + 250 mg of amoxicillin TDS and 125 clavulanate for 14 days and metronidazole 250 mg BD for 14 days .

Results: In this study by comprehensive maintenance therapy in both the groups we delay the loss of dentition of the patients of PLS. The use of antibiotics had proven to show a statistically significant difference in retaining the teeth of PLS. Patients compared to the control.

Conclusion: PLS patients, periodontitis may be arrested by combined mechanical and antibiotic periodontal treatment; extraction of severely diseased teeth; oral hygiene instructions; intensive maintenance therapy; and microbiological monitoring and treatment of the infection with *Aggregatibacter actinomycetemcomitans*.

Key words

Papillon–Lefèvre syndrome (PLS), Scaling and root planning (SRP), Periodontitis.

Introduction

Papillon-Lefèvre syndrome, first described by two French physicians Papillon and Lefèvre in 1924 [1], is an extremely rare genodermatosis inherited as an autosomal recessive trait, affecting children between the ages of 1-4 years [2, 3]. It is characterized by severe destruction of alveolar bone involving both the deciduous and permanent dentitions. Inflammatory gingival enlargement, gingival ulceration and formation of deep pockets are frequently present. In other instances there is no inflammatory element and only the permanent dentition may be affected. The characteristic skin lesions associated with the changes consist of keratotic lesions of the palmar and plantar surfaces [4]. The palmoplantar keratoderma typically has its onset between the ages of 1 and 4 years [5]. The sharply demarcated erythematous keratotic plaques may occur focally, but usually involve the entire surface of the palms and soles, sometimes extending onto the dorsal surfaces of the hands and feet. Well-demarcated psoriasis form plaques occur on the elbows and knees [6]. Often, there is associated hyperhidrosis of the palms and soles resulting in a foul-smelling odor [3]. The findings may worsen in winter and be associated with painful fissures. Another feature of PLS may be radiographic evidence of intracranial calcification [7].

Aim

- Evaluation of periodontal status in patients with Papillon–Lefèvre syndrome (PLS) observed for ≥5 years.
- Treatment of patients of PLS with SRP and maintenance for a period of ≥5 years.
- Comparing the effects of treatment of periodontitis in (PLS) patients with SRP (scaling and root planning) as a monotherapy with antibiotics as an adjunct.

Materials and methods

All subject showing signs and symptoms of PLS, were selected for this study comprising of both the sexes, visiting outpatient department of Periodontology, Govt. Dental College and Hospital Srinagar. Eight patients (aged 5-12 years) from five families (three pairs of siblings) were included. Subjects were randomly distributed into two groups 4 patients each. Control group - Group A (SRP + Placebo) and Treatment group - Group B (SRP + 250 mg of amoxicillin TDS and 125 clavulanate for 14 days and metronidazole 250 mg BD for 14 days).

Both the groups of the patients test and control were treated with SRP in the beginning of the study. Test group was thereafter put on antibiotics 250 mg of amoxicillin TDS and 125 clavulanate for 14 days and metronidazole 250 mg BD for 14 days. Maintenance therapy was instilled with recall once every month for a period of 6 months then once every 3 months for a period of 5years or more for both the groups A and B. At each appointment the relative attachment loss was recorded.

Results

On comparison between the two groups at the baseline the difference of relative attachment level was statistically not significant. The control group (group A) showed greater loss of attachment levels than test group (group B) after 1 year of study. Hence, the relative attachment level measurements taken at 1year showed greater values in (group A) than (group B). The results showed a statistically significant difference at 1 year (p 0.012).

After comprehensive periodontal therapy in eight PLS patients, teeth were retained in only two, both of which belonged to the Test group B at the end of 5 years. In six patients, all teeth were extracted, almost entirely due to periodontal

reasons. Patients' teeth were prosthodontically restored (**Figure – 1 to 4**, **Table – 1**).

Figure - 1: Dentition of a PLS patient of age 13 years.

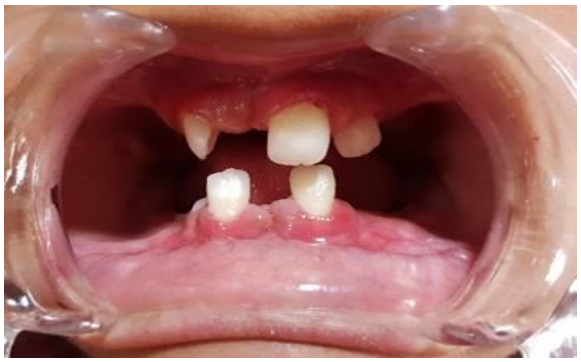


Figure - 2: Mild calcification dura mater in patient of PLS.

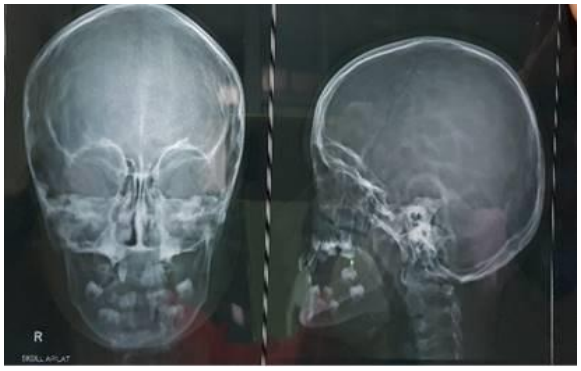
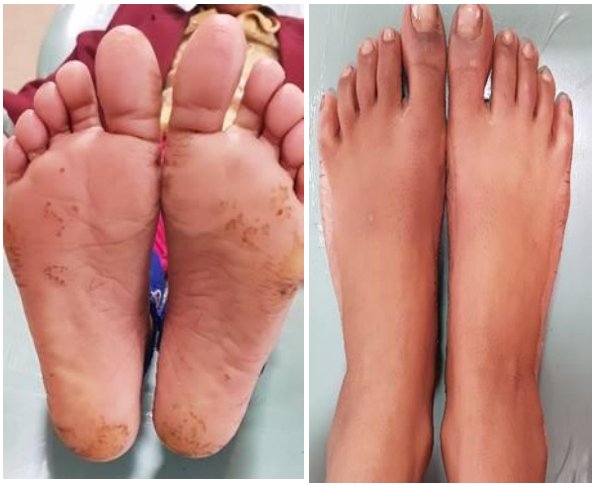


Figure - 3: Collapsed lips and cheeks in patient of PLS.

Discussion

Papillon-Lefèvre syndrome (PLS) is an autosomal recessively inherited member of the large group of palmoplantar ectodermal dysplasias, characterized by palmoplantar hyperkeratosis and severe periodontitis. The prevalence of PLS is reported to be 1 to 4 per million population [8]. Males and females are equally affected and there is no racial predominance [1].

Figure - 4: Plantar keratoderma.



The major feature of PLS is severe periodontitis, which starts at age 3 or 4 years [6]. The development and eruption of the deciduous teeth proceeds normally, but their eruption is associated with gingival inflammation and subsequent rapid destruction of the periodontium. The resulting periodontitis characteristically is unresponsive to traditional periodontal treatment modalities and the primary dentition is usually exfoliated prematurely by age 4 years. After exfoliation, the inflammation subsides and the gingiva appears healthy. However, with the eruption of the permanent dentition, the process of gingivitis and periodontitis is usually repeated and there is subsequent premature exfoliation of the permanent teeth, although the third molars are sometimes spared [1]. The degree of dermatologic involvement may not be related to the level of periodontal infection [9]. Nail changes are apparent in advanced cases as in this case, manifested by transverse grooving and fissuring [10]. In addition to the skin and oral findings, patients may have decreased neutrophil, lymphocyte, or monocyte functions and an increased susceptibility to bacteria, associated

with recurrent pyogenic infections of the skin. Pyogenic liver abscess is increasingly recognized as a complication of PLS associated with impairment of the immune system [1].

Two research groups have reported that loss-of-function mutations affecting both the alleles of the cathepsin-C gene, located on chromosome 11q14.1-q14.3, were associated with PLS [11, 12]. The cathepsin-C gene encodes a cysteine-lysosomal protease also known as dipeptidyl-peptidase I, which functions to remove dipeptides from the amino terminus of the protein substrate. It also has endopeptidase activity. The cathepsin-C gene is expressed in epithelial regions commonly affected by PLS such as palms, soles, knees, and keratinized oral gingiva. It is also expressed at high levels in various immune cells including polymorphonuclear leukocytes, macrophages, and their precursors. Several mutations have been reported in the cathepsin-C gene in individuals from diverse ethnic groups [13]. The exact cause of the periodontal disease in PLS has not been found but it has been attributed to decreased neutrophil phagocytosis, bacterial infection and impaired reactivity to T- and B-cell mitogens. The exact mechanism of the increased susceptibility to infections is also unknown, but some investigators have demonstrated a dysfunction in neutrophil motility and bactericidal function [1, 14]. It would be pertinent to mention that there are reports of at least six cases of late-onset variation of PLS without underlying cathepsin-C gene mutations [15].

Table - 1: Comparison of changes in Mean Relative Attachment Levels between two groups.

Relative Attachment Level	**Group A**		**Group B**		**Difference between groups**	**P-value**
	Mean	**SD**	**Mean**	**SD**		
Baseline	12.82	0.151	12.89	0.062	0.07	0.146#
1Year	15.26	0.343	14.93	0.332	0.33	0.012*

***Statistically Significant Difference (P-value by Independent t-test)**
#Statistically Non-significant Difference (P-value by Independent t-test)

The etiology of PLS is still unknown. Following factors have been proposed:

1. Impairment of neutrophil chemotaxis, phagocytosis, and bactericidal activities accompanied in by a decrease cell migration [1, 16]
2. Virulent Gram-negative anaerobic pathogens (actinobacillus actinomycetemcomitans) in the periodontal plaques and in periodontal pockets might act as trigger factors [17]
3. Dysfunction of immune system including reduced lymphocyte response to pathogens, depression of helper/suppressor T cells ratio, deficient monocytic function, elevation of serum IgG, and degenerative changes of plasma cells [18, 19].

Microbial aspects

Neutrophil-function test in PLS showed reduced response to *Staphylococcus* spp. and *A. actinomycetemcomitans.* There is a hypothesis that herpes viruses together with pathogenic bacteria including *A. actinomycetemcomitans* and underlying host defence disorders participate in the development of PLS periodontitis. Existence of various virulence factors, such as leukotoxin, collagenase, endotoxin, epithelial toxins, and fibroblast-inhibiting factor, suggests that PLS is mediated bacteriologically. The serum from affected patients shows high immunoglobulin G titer against *A. actinomycetemcomitans*. Moreover, *A. actinomycetemcomitans* colonies were cultured in high percentages from the periodontal pocket samples.

A multidisciplinary approach is important for the care of patients with PLS. The periodontitis in PLS is usually difficult to control. Effective treatment for the periodontitis includes extraction of the primary teeth combined with oral antibiotics and professional teeth cleaning. A course of antibiotics should be tried to control the active periodontitis in an effort to preserve the teeth and to prevent bacteremia and subsequently pyogenic liver abscess. The risk of pyogenic liver abscess should be kept in mind in evaluating these patients when they present with fever of unknown origin [1].

Therefore In this study by comprehensive maintenance therapy in both the groups we delay the loss of dentition of the patients of PLS. The use of antibiotics have proven to show a statistically significant difference in retaining the teeth of PLS Patients compared to the control as it targets the Virulent Gram-negative anaerobic pathogens (actinobacillus actinomycetemcomitans). The aggressive form of periodontitits seen in PLS is thus seen to benefit from the antibiotics given in the study this can be explained by decreased loss of attachment seen in test group B, thus there is statistically significant difference between the RALs between the two groups.

Conclusion

PLS threatens children and their parents with the prospect of edentulism if left untreated. Hence, early diagnosis and intervention are essential. Many treatment strategies have been evaluated for functional and esthetic dentition in dental practice. Damage of the primary or permanent dentition in PLS patients is an inevitable outcome of the disease. Complete oral rehabilitation by improving the oral hygiene and replacement of all the missing teeth can greatly reduce the morbidity and improve the lifestyle of the patient. Prosthetic replacement in PLS is age specific, specialty job involving initial replacement with complete or partial denture with future consideration for implant supported prosthesis [21]. Awareness of this syndrome is essential, if the dentist is to provide appropriate and comprehensive dental care.

In some PLS patients, periodontitis may be arrested by: combined mechanical and antibiotic periodontal treatment; extraction of severely diseased teeth; oral hygiene instructions; intensive maintenance therapy; and microbiological monitoring and treatment of the infection with *Aggregatibacter actinomycetemcomitans*. Treatment of PLS patients has always to be considered as high-risk cases. The present case reports indicated that in some patients suffering from Papillon-Lefèvre syndrome periodontal disease may be arrested by means of (i) oral hygiene instruction, (ii) extraction of severely diseased teeth, (iii) scaling root planning, (iv) systemic antibiotics. Patient motivation and education and diagnosis at an early age is very beneficial for the patient.

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