CASE REPORT

Papillon–Lefévre syndrome

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ABSTRACT

The goal of periodontal therapy has always been regeneration of the lost tissues. However, conventional periodontal therapy has not always been successful in achieving regeneration, especially when it is part of a syndrome. This case report involves a 13-year old male patient with the chief complaint of mobile teeth for over 3 months. His dental history revealed early loss of primary dentition, around 3–4 years of age and that he noticed mobility of permanent incisors and molars at 9–10 years.Keratotic skin lesions on the palms and soles were present since the age of 3 years. Full mouth intra-oral periapical radiographs showed extensive bone loss upto apical thirds of the teeth and an orthopantamograph showed "floating in air" appearance. Further, a lateral cephalogram was taken to rule out any calcifications of the duramater. The case was provisionally diagnosed to be Papillon Lefévre syndrome. A conventional polymerase chain reaction assay was also done to assess the virulence genes in aggressive periodontitis. Though the management of PLS involves the regular phases of periodontal therapy, namely, etiotropic, surgical, restorative and maintenance phases, the complete esthetic and functional rehabilitation also involves other specialities especially prosthodontic and dermatologic and later an implantologist. After appropriate periodontal and prosthodontic management, the patient has been followed up for over a year and is maintaining in a stable condition.

Key words: Generalized aggressive periodontitis, neutrophil function tests, Palmoplantar hyperkeratosis, Papillon-Lefévre syndrome, polymerase chain reaction

INTRODUCTION

"Palmoplantar keratoderma" refers to a heterogeneous group of disorders, characterized by thickening of the palms and soles. They can be hereditary, acquired, or associated with syndromes. In 1924, two French physicians Papillon and Lefévre[1] described a brother and sister with a condition characterized by palmoplantar hyperkeratosis associated with severe, early-onset periodontitis and premature loss of primary and permanent teeth. The inheritance is autosomal recessive and consanguinity is a notable feature in many patients. Other features of the syndrome which have been reported less frequently include psoriasiform plaques of the elbows and knees, nail changes, calcification of the dura, and recurrent pyogenic skin infections. This disease usually has its onset between the ages of 1 to 4 years. Males and females are equally affected. There is no racial predominance. Its prevalence is estimated to be 1 to 4 per million in the general population with a carrier rate of 2 to 4 per 1000.[2] In this case report, we highlight the multidisciplinary approach to treatment and the various investigations that were done to confirm the diagnosis.

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CASE REPORT

A 13-year-old male patient reported to the Department of Periodontology at Sree Balaji Dental College and Hospital, Chennai, India with the chief complaints of mobile teeth, bad breath, and yellowish discharge from the gums for the past 3 months. Mobility was present for the past 3 months, which increased during mastication. His dental history revealed early loss of primary dentition, around 3–4 years of age and that he noticed mobility of permanent incisors and molars at 9–10 years. Skin lesions were noticed on the palms and soles since the age of 3 years. He was the only member affected in his family among his three siblings of parents of consanguineous marriage.

Figure 1: Facial view of patient

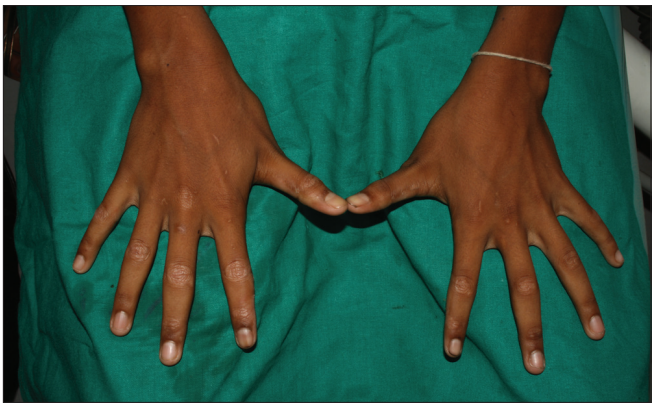

Figure 2: Hyperkeratotic patch on fingers

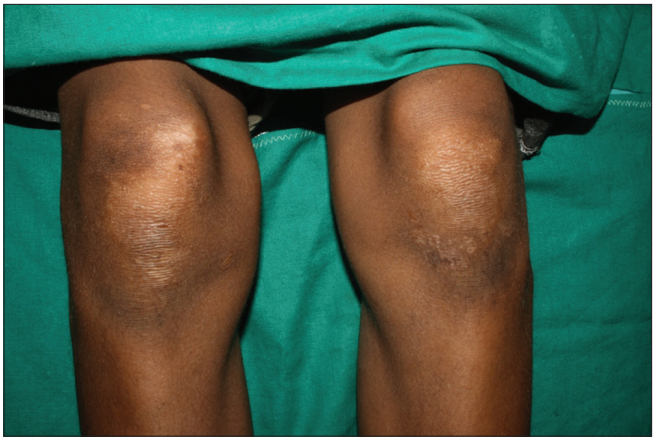

Figure 3: Hyperkeratotic patches on kness

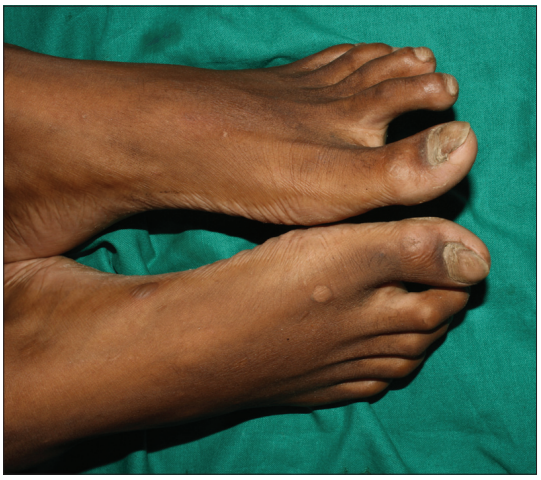

Figure 4: Lesions on feet

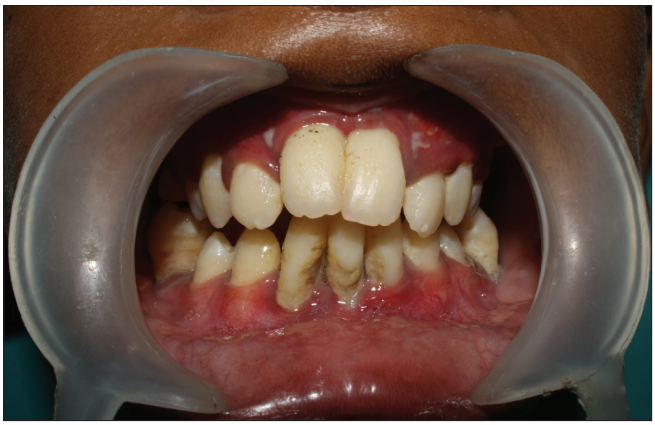

Figure 5: Facial view of lower anterior teeth showing gingival recession and inflammation

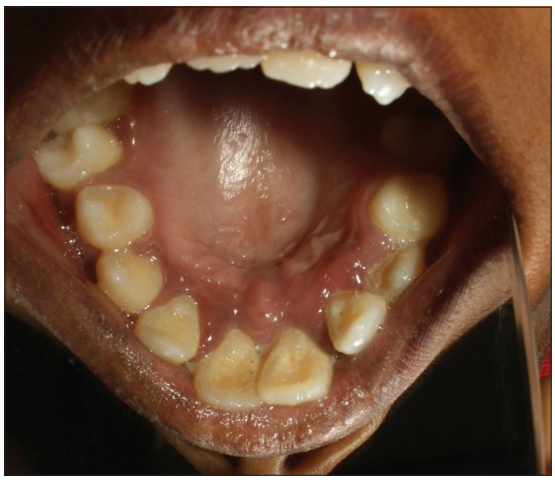

Figure 6: Palatal view of upper anterior teeth

General examination revealed that the patient was malnourished, anaemic [Figure 1] and showed presence of distinguishable hyperkeratosis at the phalanges of hands and feet, [Figures 2 and 3] elbow, and knee, [Figure 4] from normal skin. The bilateral submandibular and submental lymph nodes were tender and palpable. Intraoral examination revealed that the gingiva was bright red in appearance in relation to upper and lower anteriors and 36, 46 [Figures 5-7]. It was soft and edematous in 12, 11, 21, 22, 23, and 24. Gingival recession was present in relation to lower anteriors. The absence of stippling was prominent and there was a generalized bleeding on probing. Teeth numbers 36 and 46 showed grade IV furcation involvement. Probing depths were above 10 mm in relation to upper and lower anteriors and 36, 46. Hard tissue

examination revealed that 23 teeth were present with 41, 16, and 26 missing. Inflammation, pus discharge, and grade III mobility were also present. His oral hygiene index was inferred to be poor.

Investigations were as follows:

1. Hematological;
2. Hormone assays;
3. Height and weight;
4. Radiological investigations – Orthopantamograph, intraoral x-rays and lateral cephalogram;
5. Neutrophil function test; and
6. Conventional polymerase chain reaction (PCR) for microbiological analysis.

The patient's blood profile was found to be normal. As he had a stunted growth, assessment of insulin-like growth factor, T3, T4, and TSH were performed, and were within limits. The patient's height and weight was also calculated periodically.

Neutrophil function tests

The neutrophil function was assessed under the nitroblue tetrazolium test. It is a qualitative test using stimulated and unstimulated cells. The neutrophil migration rate was 63%, which was well within the normal range of 60–80%. The phagocytosis and respiratory burst were also normal.

Microbiological findings

Sample collection

The subgingival plaque was collected from the mesiobuccal aspect of 16, 26, 36, and 46 using a Gracey curette after careful the removal of supragingival plaque with a sterile cotton roll. The sample was transferred immediately to 500 µl of sterile phosphate buffered saline (PBS) and transported to the laboratory for storage at –20°C till assay.

As the patient was clinically diagnosed to be a case of generalised aggressive periodontitis, the red complex group (*Porphyromonas gingivalis*, *Tannerella forsythia* and *Treponema denticola*) and *Aggregatibacter actinomycetemcomitans* were screened. Since the sample showed the presence of *16s rRNA* gene of *A. actinomycetemcomitans*, further detection of two virulence genes such as *fap* and *lkt* A was performed by polymerase chain reaction (PCR).

DNA extraction

The DNA extraction from subgingival plaque sample was performed by boiling - lysis method and the supernatant were used as template for the PCR reaction.

PCR primers and amplification

The primer sequences specific for the *A. actinomycetemcomitans16S rDNA* gene are: 5′-GCT AATACC GCG TAG AGT CGG-3′ (forward), and 5′-ATTTCA CAC CTC ACT TAA AGG T-3′ (reverse)[3], for the *A. actinomycetemcomitans lktA* gene: 5′-TCG CGA ATC AGC TCG CCG-3′ (forward), and 5′-GCT TTG CAA GCT CCT CAC C-3′ (reverse)[4], and for the *A. actinomycetemcomitans fap* gene: 5′-ATT AAATAC TTT AAC TAC TAA AGC-3′ (forward), and 5′-GCA CTG TTA ACT GTA CTA GC-3′ (reverse).[5] The primer sequences specific for

1. *Porphyromonas gingivalis16S rRNA* gene are: 5′ AGGCAGCTTGCCATACTGCG-3′ (forward) and 5′ -ACTGTTAGCAACTACCGATGT-3′, (reverse)
2. *Tannerella for sythia*5′-GCGTATGTAACCTGCCCGCA-3′ (forward) and TGCTTCAGTGTCAGTTATACCT (reverse)
3. *Treponema denticola* 5′-TAATACCGAATGTGCTCA TTTACAT-3′ (forward) 5′-TCAAAGAAGCATTCCC TCTTCTTCTTA-3′ (reverse)[6] (Ashimoto *et al*., 1996)

PCR amplification was performed in a volume of 50 µl PCR mix (45 µl) contained 5 µl of 10× PCR buffer (20 mmol/L Tris-HCl, 50 mmol/L KCl, pH 8.4), 1.25 unit *Taq* DNA polymerase, 0.2 mM of each of deoxyribonucleotides, 1.5 mM MgCl2, 50pmol of primers, to which 5 µl of the template was added.

To detect *fap* and *lktA* gene of *A. actinomycetemcomitans*, PCR amplification was performed in a volume of 50 µl containing5 µl of the template, 5 µl PCR buffer (20 mmol/L Tris-HCl, 50 mmol/L KCl, pH 8.4) and 1 U Taq polymerase (Bangalore genei), 0.25 mmol/L of each dNTP, 2.5 mmol/L MgCl2, 50 pmol primers for the *A. actinomycetemcomitans fap* gene and 25 pmol primers for the *A. actinomycetemcomitans lktA* gene.

PCR products were subjected to 1.5% agarose gel electrophoresis in Tris–Borate EDTA buffer. The gel was stained with 0.5 µg/ml ethidium bromide and photographed under Biorad UV gel documentation system. A 100 bp ladder served as the molecular weight marker. The PCR reactions were performed in duplicate.

Intra oral periapical radiographs

Presence of horizontal bone loss upto apical 1/3rd in relation to upper and lower anterior teeth and 36,46 [Figure 8].

A digital orthopantamograph revealed characteristic "floating in air" appearance, which indicates severe resorption of alveolar bone [Figure 9].

Lateral cephalogram

No evidences of intracranial calcification[7] [Figure 10].

Provisional diagnosis

Correlating the clinical features of palmar plantar

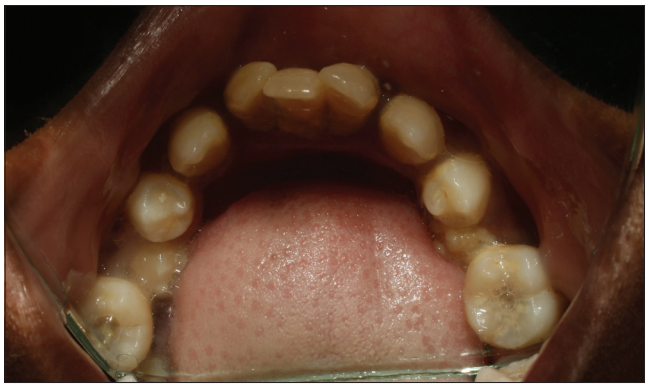

Figure 7: Lingual aspect of lower anteriors

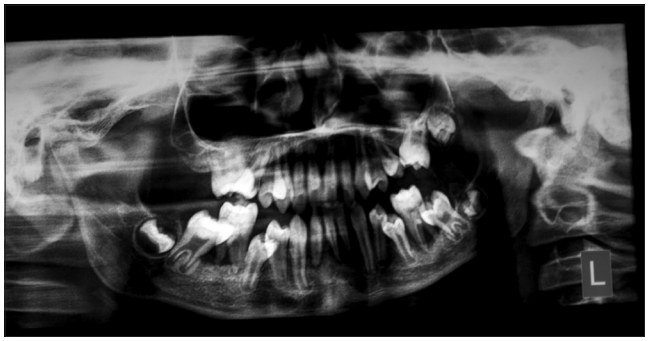

Figure 9: Orthopantamograph of patient showing "floating in air" appearance

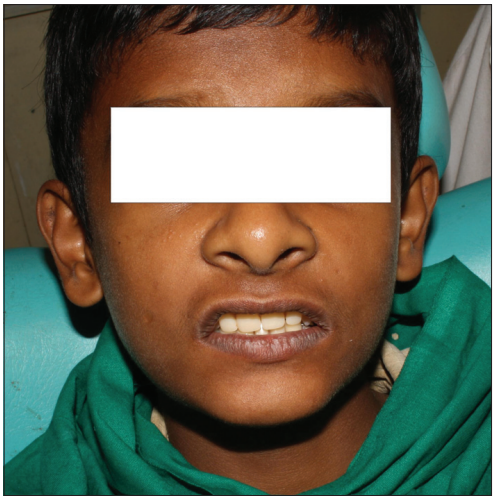

Figure 11: Facial view after restoration with a flexible partial denture, replacing the missing teeth

hyperkeratosis and the generalized aggressive nature of periodontitis, the case was provisionally diagnosed to be Papillon–Lefevre syndrome.

Differential diagnosis

1. Haim–Munk syndrome,
2. Nonsyndromic prepubertal periodontitis, and
3. Generalized aggressive periodontitis

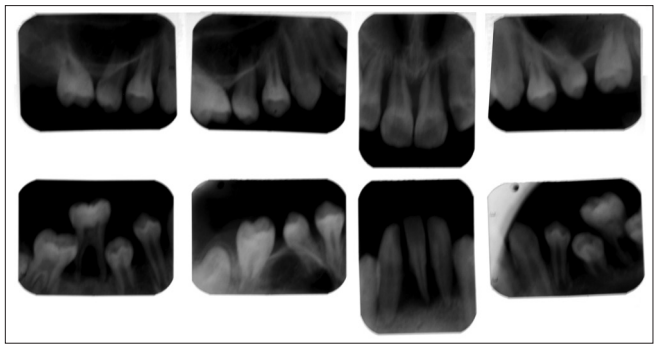

Figure 8: Full mouth intraoral periapical radiographs showing bone loss up to apical one-thirds of teeth

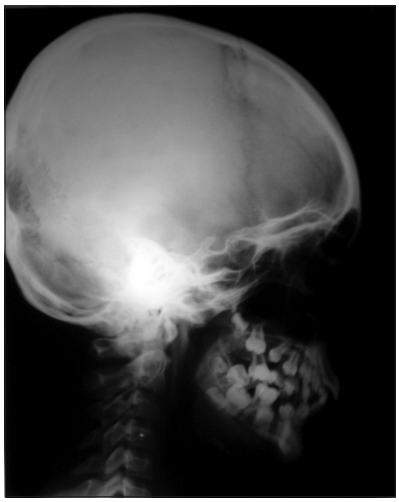

Figure 10: Lateral cephalogram showing no evidence of intracranial calcifications

Periodontal treatment

Emergency phase

Extraction of 11, 12, 21, 22, 31, 32, 42, 36 and 46.

Phase I therapy: Scaling and root planing of the remaining teeth.

Phase III: Replacement of missing teeth initially with flexible removable partial dentures [Figure 11].

Phase IV: Periodic maintenance recall and review.

DISCUSSION

PLS patients have an increased susceptibility to bacterial infection of the periodontium. The susceptibility factor may involve defective immune function or pleiotropic effect of the single mutant Cathepsin C gene.[8] There are also data to suggest epithelial aberrations. An absence of 64–kDa and a significant increase in 56– to 58–kDa keratins were found when compared to healthy controls. The neutrophil function test values were found to be within normal limits. Though this was in contradiction to the reduced neutrophil chemotaxis usually exhibited by patients with PLS[9] (VanDyke, 1984), studies by Lyberg in 1982 have shown a normal rate of

neutrophil chemotaxis[10] This was attributed to the difference in the method used to assess the same.

The management of PLS is challenging to the periodontist as the prognosis is poor and the course of the disease is unpredictable. Prior to 1980, tooth loss was considered to be an inevitable sequel to PLS. However, with the development of techniques for identifying periodontal pathogens and the ability to monitor patients before and after therapy, clinicians started to evaluate specific protocols for the treatment of the periodontal component of PLS. Now early treatment and compliance with the prevention program are the major determinants for preserving permanent teeth in young PLS patients. By extracting all primary teeth and eradicating periodontal pathogens, the patient's adult teeth can erupt into a safe environment. Treatment may be more beneficial if it is started during the eruption and maintained during the development of the permanent teeth. Recommended therapy now includes aggressive local measures to control plaque including rigorous oral hygiene, chlorhexidine mouth rinses, frequent professional prophylaxis, and periodic appropriate antibiotic therapy[11,12] needed for long-term maintenance. The periodontitis in PLS is usually difficult to control. It is reported that etretinate and acitretin modulate the course of periodontitis and preserve the teeth.[13,14] Unfortunately, etretinate is not without complications. Adverse side effects may include dryness of lips, mild pruritis, transient hair loss, elevated serum triglycerides, and liver enzymes, hypervitaminosis A, teratogenicity, and liver toxicity. Pyogenic liver abscess is increasingly recognized as a complication of PLS because of impairment of the immune system.[15] The risk of pyogenic liver abscess should be kept in mind in evaluating these patients when they present with fever of unknown origin.

PLS however, needs to be differentiated from other syndromes and also other conditions showing similar oral and cutaneous clinical features such as acrodynia, hypophosphatasia, Histiocytosis X, leukemia, cyclic neutropenia, and Takahara syndrome. They are also associated with periodontitis and early loss of teeth, but do not have the characteristic palmoplantar keratosis. The Haim–Munk syndrome is an unusual condition of palmoplantar keratosis, early-onset periodontitis, arachnodactyly and recurrent abscesses. Bullon *et al*.,[16] reported that there is a clinical variation of the skin lesions from slight to severe. In this case, report too, the keratosis was not severe, as in classical cases but fell into the moderate category.

CONCLUSION

The diagnosis of Papillon–Lefévre syndrome is unique to its clinical characteristics. However, the management from a periodontal point of view appears to follow the routine phases of periodontal therapy, with special emphasis on the periodic recall review and maintenance of the individual with systemic antibiotics when deemed necessary. The syndrome can reduce the self-confidence of the patient at a very early age and thus oral rehabilitation must take the forefront. Though initial replacement is with removable partial dentures, future consideration must be given for implant-supported prostheses.[17] The complete rehabilitation of both periodontal health and functional esthetics is thus an interdisciplinary approach which improves the morale of the patients and parents.

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