

Papillon-Lefèvre Syndrome: A Case Report

*Authored by Mohammad Hosein Kalantar Motamedi, DDS,
Ali Lotfi, DMD, Taghi Azizi, DMD and Mohammad Moshref, DMD*

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Papillon-Lefèvre Syndrome: A Case Report

LEARNING OBJECTIVES:

After reading this article, the individual will learn:

- Diagnosis of the patient with Papillon-Lefèvre Syndrome (PLS).
- Treatment of PLS by the dental practitioner and other specialists.

ABOUT THE AUTHORS



Dr. Motamedi is professor of Oral and Maxillofacial Surgery, Trauma Research Center, Baqiyatallah University of Medical Sciences, and attending surgeon, Azad University of Medical Sciences, Tehran, IR Iran. He can be reached at motamedical@lycos.com.

Dr. Motamedi does not report any disclosures.

Dr. Lotfi is assistant professor of Oral and Maxillofacial Pathology, Department of Pathology, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran.

Dr. Lotfi does not report any disclosures.

Dr. Azizi is assistant professor of Oral and Maxillofacial Pathology, Department of Pathology, Baqiyatallah University of Medical Sciences, Tehran, IR Iran.

Dr. Azizi does not report any disclosures.

Dr. Moshref is associate professor of Oral and Maxillofacial Pathology, Department of Pathology, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran.

Dr. Moshref does not report any disclosures.

INTRODUCTION

Papillon-Lefèvre Syndrome (PLS) is a rare autosomal recessive disorder characterized by palmar-plantar hyperkeratosis that may accompany psoriasiform plaques on the extensor surfaces, severe periodontitis, and premature loss of deciduous and permanent teeth. In addition to the dermatologic and oral findings, patients may have decreased function of neutrophils, lymphocytes, or monocytes and an increased susceptibility to bacterial infection, leading to recurrent pyogenic infections of the skin. Pyogenic liver abscess is a complication of PLS and is associated with impairment of the immune system.¹ Another feature of PLS is the presence of radiographic evidence of intra-cranial calcification in the choroid plexus and tentorium.^{1,2} PLS is caused by mutations in the cathepsin C (CTSC) gene.³⁻⁷ Several mutations have been reported in this gene, causing PLS.

Papillon and Lefèvre⁸ described the syndrome that bears their name in 1924.⁸ They reported a brother and a sister with palmoplantar hyperkeratosis associated with severe early-onset periodontitis and premature loss of primary and permanent teeth. PLS is a rare condition, characterized by autosomal recessive transmission. Because of autosomal recessive inheritance pattern, the parents are not typically affected. Consanguinity is noted in approximately one third of cases.⁹ The prevalence of PLS is 1 to 4 per million with no sex predilection and no racial predominance, and the disease becomes apparent by 2 to 3 years of age. Carriers are thought to be present in 2 to 4 per thousand individuals.⁸ The soles of the feet are severely affected, and erythema always precedes hyperkeratosis. The hands are also affected, but to a lesser degree.^{9,10} The sharply demarcated, erythematous keratotic plaques involve the entire surface of the palms and soles, sometimes extending onto the dorsal surface of the hands and feet. The lesions are punctate and diffuse, with dry scaly skin, and vary in thickness from one to several millimeters. Psoriasiform plaques may also be seen on the elbows and knees. The symptoms may worsen in winter and be associated with painful fissures.

Severe periodontitis associated with PLS starts at the age of 3 to 4 years. The eruption of primary teeth occurs at

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the expected ages and in the normal sequence, with the teeth being of normal form and structure, but their eruption is associated with severe gingival inflammation in the absence of any local etiologic factor. The gingiva is bright red, edematous, and bleeds easily. The rest of the oral mucous membrane is reported to be completely normal.^{9,11} A rapid loss of attachment occurs, with the teeth soon lacking osseous support and radiographically appearing to float in the soft tissue or to be “floating-in-air.”¹¹

The primary dentition is usually exfoliated prematurely by the age of 4 years. After exfoliation, the inflammation subsides and the gingiva appears healthy. With the eruption of permanent dentition, the entire process of gingivitis and periodontitis is repeated and there is subsequent premature exfoliation of the permanent teeth by the age of 12 to 15 years. Later, the third molars undergo the same process.^{1,2}

A multidisciplinary approach is necessary in the management of patients with PLS. The periodontal disease may be arrested by improving oral hygiene, extraction of severely diseased teeth, scaling, systemic antibiotics, and long-term antimicrobial irrigation.¹²

This article presents a case report involving the diagnosis and management of a young patient with PLS.

CASE REPORT

A 14-year-old male patient presented via referral with a complaint of generalized inflammation and swelling of the gingiva accompanied by bleeding and infection, 2 lost teeth, and mobility of remaining teeth. Further, the patient complained of



Figure 1. Multiple hyperkeratotic lesions affecting entire surface of the palms and soles and the dorsal surface of the fingers.



Figure 2. Psoriasiform plaques on the elbows and knees.

Figure 3. Inflamed and edematous gingiva.

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hyperkeratotic lesions on the hands and feet, including involvement of the nails, and psoriasiform plaques on the elbows and knees.

Physically, the patient appeared to be short structured. Examination revealed extensive and multiple hyperkeratotic lesions affecting the entire surface of the palms and soles, and the dorsal surface of the fingers (Figure 1). Psoriasiform plaques were noted on the elbows and knees (Figure 2). Intraoral examination revealed that the maxillary central incisors were missing, and severe mobility was present in the existing teeth, with deep periodontal pockets and bleeding on probing. The gingiva was inflamed and edematous (Figure 3). Radiographs revealed destruction of the alveolar bone around the residual teeth, resulting in some teeth having a “floating in air” appearance (Figure 4).

Consanguinity was noted between the patient’s parents. Of the 4 children in this family (2 boys and 2 girls), one male (the present case) was noted for PLS and one female was noted for congenital renal disease.

Management of the acute phase of the disease consisted of administering amoxicillin 500 mg plus metronidazole 250 mg every 8 hours for 10 days to treat periodontal abscesses. Mobile teeth were extracted. Periodic scaling and prophylaxis, and chlorhexidine rinses, were administered to manage the periodontal problems associated with the disease. Skin lesions were treated with oral acitretin 25 mg daily for 3 months initially, and periodically thereafter to control symptoms. The patient has remained stable under the care of a dermatologist for several years.

DISCUSSION

In the case presented, the dermatological and periodontal features strongly suggested the diagnosis of PLS. Dermatological features were severe. Other sites that

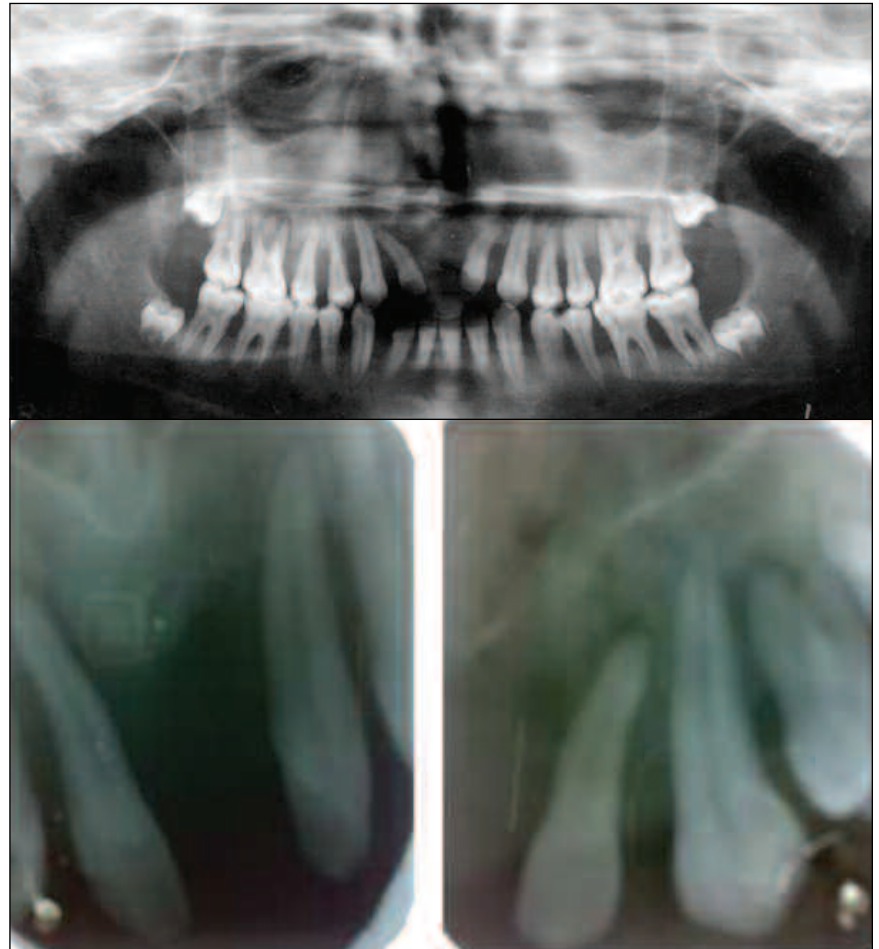


Figure 4. Radiographic examination revealing destruction of the alveolar bone around the residual teeth, giving some teeth a ‘floating in air’ appearance.

may be affected include the eyelids, cheeks, labial commissures, legs, thighs, and axillae. The hair is usually normal, but in advanced cases the nails may show transverse grooving and fissuring. Histopathologic examination reveals nonspecific hyperkeratosis, acanthosis, focal parakeratosis, psoriasiform hyperplasia, tortuous capillaries in dermal papillae, and superficial lymphocytic infiltration.^{1,11,13}

Although the case reported here was associated with consanguinity of the parents, the parents were phenotypically healthy. PLS is caused by mutations in the CTSC gene. Several mutations have been reported in this gene, causing PLS. Due to gene mutations, PLS cases typically demonstrate greatly accelerated onset and

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progression of periodontitis. CTSC is a lysosomal cysteine proteinase. PLS patients demonstrate more than a 90% reduction of CTSC activity. This gene is important in the structural growth and development of the skin, and is critical for appropriate immune response of myeloid and lymphoid cells. Loss of appropriate function of the CTSC gene is thought to result in an altered immune response to infection. An increased susceptibility to infection has also been reported in approximately 25% of PLS patients. In addition, the altered gene may affect the integrity of the junctional epithelium surrounding the tooth.^{3-7,14}

The case presented had prototypical findings including fingernail anomalies and skin problems affecting both the dorsal and ventral surfaces of the extremities as well as on the elbows and knees. These manifestations may relate to the degree that the gene is phenotypically expressed. Other cases encountered by the authors did not have manifestations to this extent. Less frequent findings include involvement of the skin of the axilla, arms, and legs.

Although there is a hereditary component and leukocyte dysfunction can be demonstrated, it appears that there must be an infection with a specific, potent bacterium, such as *Actinobacillus* (*Aggregatibacter*) *actinomycetemcomitans*, for the periodontal component to develop.¹ Pre-pubertal periodontitis is associated with loss of CTSC enzyme activity.^{3,5-7} These immunologic deficiencies are transitory and appear to be related to subgingival infection by periodontal pathogens, particularly *A. actinomycetemcomitans*.¹⁰

PLS needs to be differentiated from other conditions showing similar oral and cutaneous clinical features, such as acrodynia, hypophosphatasia, histiocytosis X, leukemia,

cyclic neutropenia, and Takahara syndrome, which are also associated with periodontitis and premature loss of teeth.¹⁵

There are case reports in the literature regarding successful therapy for PLS.^{10,16-18} Rigorous oral hygiene, chlorhexidine mouthrinses, frequent professional prophylaxis, and periodic appropriate antibiotic therapy are necessary for long-term maintenance of the periodontium. The most successful treatment of the skin lesions has been administration of retinoids. Although retinoids are not well tolerated in general, there are reports describing the use of systemic retinoid therapy for palmo-plantar keratoderma associated with PLS.¹⁹

CONCLUSION

Although PLS is rare, it should be differentiated from other conditions which demonstrate similar oral and cutaneous clinical features, such as acrodynia, hypophosphatasia, histiocytosis X, leukemia, cyclic neutropenia, and Takahara syndrome, which are also associated with periodontitis and premature loss of teeth.¹⁵ The most successful treatment of the skin lesions has been administration of retinoids, although it should be noted that retinoids are not well tolerated in general. On the part of the dentist, rigorous oral hygiene, chlorhexidine mouth-rinses, frequent professional prophylaxis, and periodic appropriate antibiotic therapy are to be implemented and are necessary for long-term maintenance of periodontal problems.¹⁰ Multi-specialty cooperation within dentistry and dentist-physician cooperation is required for both initial and long-term management of this disease.^{19,20}

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REFERENCES

1. Janjua SA, Khachemoune A. Papillon-Lefèvre syndrome: case report and review of the literature. *Dermatol Online J*. 2004;10:13.
2. Mahajan VK, Thakur NS, Sharma NL. Papillon-Lefèvre syndrome. *Indian Pediatr*. 2003;40: 1197-1200.
3. Toomes C, James J, Wood AJ, et al. Loss-of-function mutations in the cathepsin C gene result in periodontal disease and palmoplantar keratosis. *Nat Genet*. 1999;23:421-424.
4. Hart TC, Hart PS, Michalec MD, et al. Localisation of a gene for prepubertal periodontitis to chromosome 11q14 and identification of a cathepsin C gene mutation. *J Med Genet*. 2000; 37:95-101.
5. de Haar SF, Jansen DC, Schoenmaker T, et al. Loss-of-function mutations in cathepsin C in two families with Papillon-Lefèvre syndrome are associated with deficiency of serine proteinases in PMNs. *Hum Mutat*. 2004;23:524.
6. Pham CT, Ivanovich JL, Raptis SZ, et al. Papillon-Lefèvre syndrome: correlating the molecular, cellular, and clinical consequences of cathepsin C/dipeptidyl peptidase I deficiency in humans. *J Immunol*. 2004;173:7277-7281.
7. Zhang Y, Hart PS, Moretti AJ, et al. Biochemical and mutational analyses of the cathepsin c gene (CTSC) in three North American families with Papillon Lefèvre syndrome. *Hum Mutat*. 2002; 20:75.
8. Papillon MM, Lefèvre P. Two cases of symmetrical, familial (Meleda's malady) palmar and plantar keratosis of brother and sister: coexistence in two cases with serious dental changes [in French]. *Bull Soc Fr Dermatol Syphiligr*. 1924; 31:82-87.
9. Hattab FN, Rawashdeh MA, Yassin OM, et al. Papillon-Lefèvre syndrome: a review of the literature and report of 4 cases. *J Periodontol*. 1995;66:413-420.
10. Ikeshima A. Papillon-Lefèvre syndrome: a highly-suspected case. *J Oral Sci*. 2006;48:257-260.
11. Shah J, Goel S. Papillon-Lefèvre syndrome: two case reports. *Indian J Dent Res*. 2007;18: 210-213.
12. Rüdiger S, Petersilka G, Flemmig TF. Combined systemic and local antimicrobial therapy of periodontal disease in Papillon-Lefèvre syndrome: a report of 4 cases. *J Clin Periodontol*. 1999; 26:847-854.
13. Yagmur A, Yilmaz G, Ertan U, et al. Papillon Lefèvre syndrome: a case report. *Int Pediatr*. 2004;19:224-225.
14. Nagaveni NB, Suma R, Shashikiran ND, et al. Papillon-Lefèvre syndrome: report of two cases in the same family. *J Indian Soc Pedod Prev Dent*. 2008;26:78-81.
15. Hattab FN, Amin WM. Papillon-Lefèvre syndrome with albinism: a review of the literature and report of 2 brothers. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2005;100:709-716.
16. 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;27:354-360.
17. Pacheco JJ, Coelho C, Salazar F, et al. Treatment of Papillon-Lefèvre syndrome periodontitis. *J Clin Periodontol*. 2002;29:370-374.
18. Tinanoff N, Tempro P, Maderazo EG. Dental treatment of Papillon-Lefèvre syndrome: 15-year follow-up. *J Clin Periodontol*. 1995;22: 609-612.
19. Ahuja V, Shin RH, Mudgil A, et al. Papillon-Lefèvre syndrome: a successful outcome. *J Periodontol*. 2005;76:1996-2001.
20. de Freitas AC, Assed S, da Silva LA, et al. Aggressive periodontitis associated with Papillon-Lefèvre syndrome: report of a 14-year follow-up. *Spec Care Dentist*. 2007;27:95-100.

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POST EXAMINATION QUESTIONS

1. **Papillon-Lefèvre Syndrome (PLS) is:**
 - a. a disease acquired after birth.
 - b. an inherited disease (dominant trait).
 - c. a developmental anomaly.
 - d. an autosomal recessive disorder.
2. **The following is/are TRUE for PLS:**
 - a. It may result in rapid tooth loss.
 - b. There is radiographic evidence of intracranial calcification in the choroid plexus and tentorium.
 - c. It may damage the fingernails.
 - d. all of the above.
3. **Severe periodontitis associated with PLS:**
 - a. starts at the age of 3 to 4 years.
 - b. starts at the age of 5 to 7 years.
 - c. starts at the age of 8 to 9 years.
 - d. starts at the age of 10 to 14 years.
4. **PLS patients show:**
 - a. abnormal tooth form + loosening of the dentition.
 - b. normal tooth form + premature loss of teeth.
 - c. tooth impaction + loosening of the dentition.
 - d. abnormal hair + tooth exfoliation.
5. **PLS patients show similarities to:**
 - a. acrodynia.
 - b. histiocytosis X.
 - c. leukemia.
 - d. all the above.
6. **Histopathologic examination of samples of PLS patients show:**
 - a. nonspecific hyperkeratosis.
 - b. psoriasiform hyperplasia.
 - c. superficial lymphocytic infiltration.
 - d. all the above.
7. **PLS is caused by:**
 - a. mutations in the cathepsin C (CTSC) gene.
 - b. C-reactive protein.
 - c. lack of vitamin C.
 - d. none of the above.
8. **For the periodontal component of PLS to develop it appears that there must be an infection with a specific, potent bacterium such as:**
 - a. Actinobacillus (Aggregatibacter) actinomycetemcomitans.
 - b. Actinomycosis bovis.
 - c. Streptococci.
 - d. none of the above.

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