

CASE REPORT

PAPILLON-LEFÈVRE SYNDROME: clinical presentation and literature review

Taiwo OA¹, Adeyemi MO², Adeyemo WL², Ogunlewe MO², Ladeinde AI²

¹Department of Surgery, College of Health Sciences Usmanu Danfodiyo University Sokoto, Nigeria ²Department of Oral and Maxillofacial Surgery, Lagos University Teaching Hospital

ABSTRACT

BACKGROUND: Papillon-Lefèvre syndrome is a rare autosomal recessive genodermatosis characterised by a diffused palmoplantar hyperkeratosis and severe early-onset periodontitis. Although the exact pathogenesis of this syndrome is still unknown however, it has been linked to mutations in the cathepsin C (CTSC) gene. We report a case of PLS from our centre in North-western Nigeria with characteristic skin and oral lesions.

CASE REPORT: This paper is a clinical presentation of a 12 year old male with severe periodontitis with loosening exfoliation of teeth, characteristic palmoplantar hyperkeratosis and normal full blood count and liver ultrasound. Based on medical and dental findings, a diagnosis of Papillon-Lefèvre Syndrome was made.

CONCLUSION: An early diagnosis of the syndrome can help preserve the teeth by early institution of treatment, using a multidisciplinary approach. Thereby, sparing the patients increase risk of social, psychological, and economical stigma. Owing to the vast degree of periodontal breakdown involved at such an early age, the dentist is often the first to encounter such patients. This patient presented primarily because of oral lesions, hence dentists requires a high index of suspicion to pick this condition.

Key words: Papillon-Lefèvre syndrome, palmoplantar hyperkeratosis, periodontitis

Correspondence address:

Dr Taiwo Olanrewaju A.

Department of Surgery,
College of Health Sciences
Usmanu Danfodiyo
University
MB 12003, Sokoto,
Nigeria
234 8078061517
oataiwo@yahoo.com

INTRODUCTION

Papillon-Lefèvre syndrome (PLS) is a rare, autosomal recessive heterogeneous disorder, which was first described in the literature by two French physicians Papillon and Lefevre in 1924.¹ PLS is characterized by palmoplantar hyperkeratosis, early loss of primary and permanent teeth, and associated

calcification of the dura mater.^{2,3} The incidence rate of PLS is between one to four persons per million without racial or sexual predilection and greater frequency of occurrence in the consanguineous offspring has been determined in about 20 to 40% of patients with this condition.⁴ This keratinization disorder is characterized by

palmoplantar hyperkeratosis and early onset aggressive periodontitis. Other Associated features may include intra-cranial calcifications, susceptibility to bacterial infections and mental retardation.⁴ Other regions often affected by keratosis include dorsal surface of hands and feet, knees, elbows, dorsal eyelids, cheeks, thighs, labial commissures and external malleolus, although with significant variation.^{3,4}

The exact aetiology of PLS is obscured and factors such as immunologic, inflammatory and virulent pathogens has been linked to this syndrome. However, the molecular basis responsible in this condition has been elucidated.^[4] Researchers from various studies have discovered a genetic mutation in cathepsin-C gene which encodes a cysteine-lysosomal protease known as dipeptidyl-peptidase I or Cathepsin C, removing dipeptides from the amino-terminus of protein substrates and mainly plays an immune and inflammatory role.^{4,5} Variation in the clinical presentation of PLS has been observed however, cutaneous and oral lesions are characteristics.⁴ PLS usually manifests itself between the ages of 6 months to 4 years, coinciding with the eruption of primary teeth and leads to premature loss of both primary and permanent dentitions.⁶ The cutaneous lesions presenting as sharply demarcated erythematous keratotic plaques on the palms and soles, with extension to the dorsal surfaces are often manifested simultaneously with the intra-oral presentations. These cutaneous regions are more severely affected than the others sites, with erythematous presentation always preceding the hyperkeratosis.^{6,7} Histopathologic findings are nonspecific, however hyperkeratosis with irregular parakeratosis, acanthosis, and a moderate perivascular infiltrate has been described.⁸ The management of this condition requires multidisciplinary approach involving the dermatologist and dentist. Oral lesions often respond to classic periodontal treatment if instituted early.^{9,10}

To the best of our knowledge, there is no published report of patient with this syndrome from Nigeria or Africa in the literature. Hence,

we report a case of PLS from our centre in North-western Nigeria with characteristic skin and oral lesions.

CASE REPORT

A 12 year-old male patient presented to the Oral Diagnosis unit of the Department of Dental and Maxillofacial Surgery, Usmanu Danfodio University Teaching Hospital, Sokoto, with the chief complaint of missing teeth since 4 to 6 years of age and loosening of the remaining teeth. Past medical history showed concurrent infection of the skin which was reportedly managed with traditional topical agent which proved unsuccessful. Past dental history revealed it was the patient's first ever visit to the hospital as well as to a dental clinic on account of the present complaint. There was severe mobility of the deciduous teeth prior to exfoliation of each tooth about five to six months after complete eruption, the trend which was similarly observed in the permanent dentition. Patient had stopped brushing because of teeth mobility. There was associated odynophagia, pain, gingival swelling and occasional bleeding. Patient is from the rural area with low socioeconomic background and a polygamous family. He is the third of six surviving children, after four of the siblings died from similar skin and oral lesions.

On clinical examination, the patient presented with a senile facial appearance. There was symmetrical, well demarcated keratotic and confluent plaques involving the skin of the dorsal and plantar surfaces of the palms of hands (Figure 1) and soles of feet (figure 2) bilaterally, with consequent difficulty in walking due to plantar lesions on the feet. This was noticed at about the age of 2 years and observed to be more severe during cold weather. The skin was dry and rough on palpation, well-circumscribed, psoriasiform, erythematous, scaly plaques were also present on the elbows and knees bilaterally. However, the hair and the nails appear clinically normal. Intraoral examination revealed that the two centrals and lateral incisors, first and second premolars and first molar on both quadrant of the maxilla, as well as centrals and lateral incisors on both quadrant of the mandible were missing

(Figure 3). The mobile teeth include canine on both quadrants of maxilla, second premolar on the upper left, canine on the mandibular right quadrant and both premolars on the mandibular left quadrant. In addition, first and second premolars on the lower right quadrant, canine and first molar on the lower left quadrant were also mobile. They all exhibited Grade 3 mobility due to extensive bone loss and severe periodontal breakdown. The gingival in relation to the existing permanent teeth were red, soft and oedematous with associated recession, deep periodontal pocket and bleeding on probing. The overlying mucous membrane including the edentulous area appeared clinically healthy. Routine clinical investigations such as full blood count and liver ultrasound were all normal. Based on medical and dental findings, diagnosis of PLS was made. The patient was referred to the Dermatology unit of the hospital for the management of the cutaneous lesion. Scaling and polishing was instituted, however the entire patient's remaining teeth were observed to be floating given a sense of very poor prognosis. Hence, complete extraction and treatment options for prosthodontic rehabilitation were discussed. Considering the patient's age and poor socio-economic status, a set of complete dentures was planned for now with possible dental implant in future. However, the patient did not report for the outlined management of the oral condition and efforts at locating the patients' residence proved abortive.



Figure 2: Patient with dry scaly legs.



Figure 3: Patient with severe loss of teeth

DISCUSSION

Papillon-Lefèvre Syndrome has a reported prevalence of 1 to 4 cases per million.¹ The disorder is characterized by diffuse palmoplantar keratoderma and rapidly progressing periodontitis leading to premature loss of both deciduous and permanent teeth. A third component of dural calcifications has also been reported by Gorlin et al.^{1,6} Almuneef et al.¹⁰ recognize pyogenic liver abscess to be a fairly frequent complication of Papillon-Lefèvre syndrome. Dural calcification could not be ascertained



Figure 1: Patient with severe dry and scaly orsum of the hands

owing to non-affordability of computerized tomography (CT) scan (do you have plain skull X ray) and also no abnormal liver ultrasonographic finding was detected in this present case.

The characteristic dermatological lesions of symmetric palmoplantar keratosis of hands and feet including the dorsal surfaces of the extremities and others (elbows and knees) was first noticed at about the age of 2 years consistent with most reports in the literature.^{1,4,6} These lesions have been reported to be more severe during cold weather as also evidenced in this case.^{6,7} There was positive history of manifestation of recurrent pyogenic skin infections since early childhood, a finding which was also demonstrated by Subramaniam et al.¹¹ and could be attributed to the increased susceptibility to bacterial infections in these patients. Furthermore, the application of traditional ointment could also predispose patient to recurrent skin infection and perhaps aggravated it.

The intraoral presentation of severe generalised aggressive periodontitis as early as 3 to 4 years of age, following complete eruption of the deciduous teeth was observed in this case and concurred with observation in reported cases in the literature. The deciduous teeth develop normally, but their eruption is associated with severe gingival inflammation and subsequent periodontal destruction leading to a premature loss of the primary dentition, this trend was similarly noticed in this report.^{2,4,6,7} A temporary period of healthy gingival tissue was followed by another phase of destructive periodontitis once the permanent teeth erupt, as reported here with resultant potential towards partial or complete edentulous status in their early teens. This is probably the complication in this patient, which is the trend in most studies.^{1,3,4,6}

The aetiopathogenesis of Papillon-Lefèvre syndrome is relatively obscure, thereby researchers have come up with proposition such as immunologic basis whereby there is functional defect in the T-cell and natural

killer cell mediated cell killing and reduced neutrophil function secondary to reduction in chemotaxis and phagocytosis, as well as bacterial infection predominantly *A. actinomycetemcomitans* releasing leukotoxin.^{4,7} Other microbial agents including gram negative anaerobes such as *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, and *Treponema denticola* have also been suggested not only to have causal effects on the periodontal breakdown but also in the cutaneous lesions of Papillon-Lefèvre syndrome.^{1,11}

Recently, the molecular basis of PLS has been established and a genetically demonstrated loss-of-function mutations affecting both alleles of the lysosomal protease cathepsin-C gene in patients with PLS and subsequent dysregulation of localized polymorphonuclear leucocytes in inflamed periodontal tissues has been reported.^{9,13} The cathepsin-C gene, which is located on chromosome 11q14.1- q14.3 has endopeptidase activity and is expressed in epithelial regions commonly affected by PLS including palms, soles, knees, and keratinized oral gingival.^{12,13} Furthermore, high levels of expression of this gene has been found in various immune cells including polymorphonuclear leukocytes, macrophages, and their precursors.^{8,9} Haim-Munk syndrome has also been linked to mutation in cathepsin-C gene with similar characteristic palmoplantar keratosis of the hands and feet. However PLS differs from Haim-Munk syndrome in symptoms such as arachnodactyly, acroosteolysis, and onychogryphosis, which are only present in Haim-Munk syndrome.⁹ These symptoms were not observed in this case, hence Haim-Munk syndrome was ruled out. When there is premature loss of the deciduous and/or permanent teeth, one should also consider Acrodynia, a condition is usually caused by mercury intoxication which is also known as Feer's syndrome. Here, one may observe a red desquamative process involving both the

extremities. Furthermore, there is erythrocytosis, muscle pain, insomnia, sweating, tachycardia and psychic disturbances. Other differentials include: hypophosphatasia condition where teeth are prematurely shed and are hypoplastic, where increased amounts of phosphoethanolamine in the urine confirmed the diagnosis; non-syndromic prepubertal periodontitis and localized juvenile periodontitis neither of which exhibit cathepsin-C gene mutation. Other conditions to be considered in the differential diagnosis of PLS are palmoplantar hyperkeratosis of Unna Thost, mal de Meleda, Howel-Evans syndrome, keratosis punctata, keratoderma hereditarium mutilans (Vohwinkel's syndrome) and Greither's syndrome. However, while these entities are associated with palmoplantar hyperkeratosis, there is no periodontopathy.^{1,9,10} The management of PLS requires a multidisciplinary approach with the active participation of the dentist, dermatologist and pediatrician. Treatment of the oral component of the disorder must be done in concert with that of the dermatological aspect. Early recognition would help in reducing the devastating sequelae of this syndrome. Sadly, this was not the case in this report. Following the treatment protocol for periodontal therapy proposed by Ullbro et al.⁶ and Ahuja et al.,¹³ through scaling and polishing aimed at eliminating the reservoir of causative organisms was done. This we hoped would facilitate the healing of the oral tissues. Oral retinoids such as acitretin and isotretinoin have proven to be beneficial in treating both the oral and cutaneous lesions of PLS and is usually started during the eruption of permanent dentition and is followed till the normal developmental process is complete.^{7,9,10}

Unfortunately, this patient defaulted, which is understandable in African setting, where patient due to their health belief do not come back for follow up once they notice improvement in their status. In addition, the paucity of reported case in scientific literature

from Africa could be attributed to cultural value and taboo associated with consanguineous relationship. This cannot be totally ruled out in this case, as evidenced by the death of four siblings with similar skin and oral presentations.

In conclusion, an early diagnosis of the syndrome can help preserve the teeth by early institution of treatment, using a multidisciplinary approach. Thereby, sparing the patient's increase risk of social, psychological, and economical stigma. Owing to the vast degree of periodontal breakdown involved at such an early age, the dentist is often the first to encounter such patients. This patient presented primarily because of oral lesions, hence dentists requires a high index of suspicion to pick this condition.

REFERENCE

1. Muppa R, Prameela B, Dandempally A. Papillon-Lefevre syndrome: a combined approach from the Dermatologist and Dentist – a clinical presentation. *Indian J Dermatol* 2011;58(6):740-743
2. Valeshabad AK, Mazidi A, Al-Talib K. Papillon-Lefevre Syndrome: A Series of Six Cases in the Same Family. *Dermatology* doi:10.5402/2012/139104
3. Hart TC, Shapira L. Papillon-Lefevre syndrome. *Periodontology* 2000. 1994; 6:88-100.
4. Dhanrajani PJ. Papillon-Lefevre syndrome: clinical presentation and brief review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009; 108(1):1-7.
5. Yang Y, Bai X, Liu H, Li L, Cao C, Ge L. Novel mutations of cathepsin C gene in two Chinese patients with Papillon-Lefevre syndrome. *J Dent RES* 2007; 86(8):735-738.
6. Ullbro C, Crossner CG, Nederfors T, Alfadley A, Thestrup-Pedersen K. "Dermatological and oral findings in a cohort of 47 patients with Papillon-Lefevre syndrome". *J Am Acad Dermatol*. 2003; 48(3): 345-351.

7. 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(6):709–716.
8. Singla A, Sheikh S, Jindal SK, Brar R. Papillon Lefevre syndrome: Bridge between Dermatologist and Dentist. J Clin Exp Dent. 2010;2:e43–46
9. Ashri NY. Early diagnosis and treatment options for the periodontal problems in Papillon-Lefèvre syndrome: A literature review. J Int Acad Periodontol. 2008; 10:81–86.
10. Almuneef M, Al Khenazian S, Al Ajaji S, Al-Anazi A. Pyogenic liver abscess and Papillon-Lefèvre syndrome: Not a rare association. Pediatrics. 2003; 111:e85 – 88.
11. Subramaniam P, Mathew S, Gupta KK. Papillon-Lefevre syndrome: a case report. J Indian Soc Pedod Prev Dent. 2008; 26:171-174
12. Kurban M, Cheng T, Wajid M, Kiuru M, Shimomura Y, Christiano AM. A novel mutation in the cathepsin C gene in a Pakistani family with Papillon-Lefevre syndrome. J Eur Acad Dermatol Venereol. 2010; 24: 967–969.
13. Ahuja V, Shin RH, Mudgil A, Nanda V, Schoor R. "Papillon-Lefèvre syndrome: a successful outcome". J. Periodontol. 2005; 76(11): 1996–2001.