

## Case Report

# Spectrum of Papillon–Lefevre syndrome

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**Received:** 06 August 2014

**Accepted:** 06 September 2014

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### ABSTRACT

Papillon–Lefevre syndrome is an extremely rare autosomal recessive disorder characterized by severe periodontal disease with hyperkeratosis and fissuring of the palms and soles. Periodontitis is severe and destructive affecting both deciduous and permanent dentitions associated with palmo-plantar hyperkeratosis. These manifestations usually appear in childhood between 1 and 4 years of age and deciduous teeth exfoliate within or at the age of six. Permanent teeth erupt normally but soon get affected by periodontal disease. Individual becomes edentulous within teenage. Hyperkeratotic lesions extend to knees and elbows. Some cases have shown inconsistent manifestations such as calcification of falx cerebri and choroid plexus, calcification of the dura, attachment of the tentorium, thumb nail dystrophy and hyperhidrosis.

**Keywords:** Papillon–Lefevre syndrome, Palmo-plantar Keratoderma, Periodontitis

## INTRODUCTION

Papillon–Lefevre syndrome (PLS) is an autosomal recessive disorder, described by Papillon and Lefevre in 1924. Main features of PLS are hyperkeratosis of palms and soles concomitant with premature loss of primary and permanent dentition due to progressive periodontitis. Dental management of patients with PLS is usually challenging due to early excessive loss of alveolar bone support. This case report describes the salient features especially in regard palmo-plantar lesions and dental destruction in a 6-year-old child and a 23-year-old adult male patient, native of Lucknow region (Uttar Pradesh) in India.

## CASE REPORTS

### Case 1

A 6-year-old male child, born of a non-consanguineous marriage, presented to us with fissuring and thickening of skin of palms and soles (Figures 1 and 2), since 1 year.

Furthermore, there was thickening of skin of knees, bilaterally. He had exacerbation of skin lesions in the last winter season. He had recurrent episodes of bleeding and swelling from gums since birth and the deciduous teeth erupting were dystrophic and showed blackish discoloration (Figure 3). The mother stated that the deciduous teeth had to be extracted to make way for the permanent teeth. He is the elder of two siblings and was born after a full term normal delivery with normal developmental milestones. No family history suggestive of psoriasis or palmoplantar keratoderma (PPK) was elicitable.

### Examination

Dermatological examination revealed a transgrediens PPK characterized by fissuring interspersed with reddish keratotic confluent plaques of both palms and soles extending onto the dorsal surfaces. Dental examination revealed edematous gums with loss of his upper incisors, upper and lower canines, upper and lower premolars with blackish discoloration of most of the teeth. There were well-defined psoriasiform erythematous plaques

present on both the knees. There was an extensive area of xerosis on back of right thigh. No hyperhidrosis. Nails were normal.



**Figure 1: Hyperkeratosis and fissuring of palms.**



**Figure 2: Hyperkeratosis and fissuring of soles.**



**Figure 3: Dystrophic deciduous teeth showing blackish discoloration.**

### Laboratory investigations

Revealed hemoglobin of 11.1 g/dl, total leukocytes count of 9,400/mm<sup>3</sup> differential leukocyte count showed neutrophils 58%, lymphocytes 40%, eosinophils 02%, basophils 00%. Platelet count was 2.80 lakhs/mm<sup>3</sup>. Urine routine examination showed traces of proteins, 2-4 epithelial cells/hpf, occasional pus cells/hpf. Uric acid crystals were seen. Blood urea and serum creatinine were 19.0 and 0.73 mg/dl, respectively. Liver function tests revealed serum bilirubin 0.89 mg/dl with normal enzyme values. X-ray skull (lateral view) was normal. Ultrasonography of abdomen was unremarkable. Swab culture from gingiva and dystrophic teeth showed growth of *Actinobacillus actinomycetemcomitans* and *Escherichia coli*. Child refused skin biopsy.

### Diagnosis PLS

Child was exhibited a course of systemic antibiotics to control infection and explained about oral hygiene in consultation with a dentist. He has been counseled to visit the dentist once a month. Patient has been advised oral tab acitretin 10 mg once daily along with topical emollients and keratolytics. He is being monitored on a regular basis.

### Case 2

A 23-year-old male patient, born of a consanguineous marriage came to our outpatient department with chief complaints of dryness over hands and feet since infancy and thickening of palms and soles since 8 years of age



**Figure 4: Diffuse hyperkeratosis with multiple punctate depressions over the palm.**





**Figure 5: Diffuse hyperkeratosis and fissuring of soles with yellowish discoloration.**



**Figure 6: Patient with loss of permanent teeth and displaying artificial dentures.**

(Figures 4 and 5). Patient insidiously developed thickness of the hands and feet with fissuring of overlying skin especially in winters. Individual also reported dryness over elbow and knee joints. Patient stated excessive sweating over the palms and soles and absence of permanent teeth. He was using artificial dentures (Figure 6). Undertook various treatments but to no avail.

#### ***Dermatological examination***

Revealed diffuse hyperkeratosis of both palms and soles with yellowish discoloration of soles. There was foul smelling odor emanating from the feet. Hyperhidrosis was present. Fissuring over the soles and palms was seen. There were multiple punctate depressions over the palms.

Xerosis, erythema, and accentuation of markings were seen on the knee joints and over the dorsum of the foot extending till the ankle joint. Hyperpigmentation and scaling over the dorsal aspect of hands over interphalangeal joints and elbows. Mucosal examination: individual was edentulous with total loss of teeth. Patient is using dentures. Nail examination revealed loss of cuticle of nail and koilonychia. Investigations: complete blood count, liver function test, and lipid profile were within normal limits. X-ray chest was normal. X-ray of skull was also normal. Potassium hydroxide examination for fungus was negative. Orthopantomogram was advised. Treatment: patient has been advised oral tab acitretin 25 mg once daily along with topical emollients and keratolytics.

#### **DISCUSSION**

PLS was first described by two French physicians Papillon and Lefevre in 1924.<sup>1</sup> PLS is inherited as an autosomal recessive trait, affecting children between the ages 1-4 years.<sup>2,3</sup> It has the prevalence of 1-4 cases per million persons.<sup>3</sup> Males and females are equally affected and there is no racial predominance.<sup>4</sup> PLS is characterized by PPK, psoriasiform plaques of the elbows and knees, periodontal disease with resultant premature loss of deciduous and permanent teeth, and may be intracranial calcifications.<sup>5</sup> These keratotic plaques may occur focally, but more often involve the entire surface of the palms and soles.<sup>6</sup> Palmoplantar keratosis, varying from mild psoriasiform scaly skin to overt hyperkeratosis, typically develops within the first 3 years of life.<sup>7</sup> Often, they are associated hyperhidrosis of the palms and soles resulting in a foul-smelling odor.<sup>3</sup> The findings may worsen in winter and be associated with painful fissures,<sup>8</sup> as is seen in our case.

The development and eruption of the deciduous teeth and permanent dentition proceed 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 gingival 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.<sup>9</sup> The etiology of periodontal disease was explained with juvenile periodontitis due to infection with *Actinobacillus actinomycetemcomitans* rather than immunologic dysfunction or anatomic defects.<sup>6</sup> Both the deciduous and permanent dentitions are affected; resulting in premature tooth loss.

The degree of dermatologic involvement may not be related to the level of periodontal infection.<sup>10</sup>

Most PLS patients display both periodontitis and hyperkeratosis. Some patients have only palmo-plantar

keratosis or periodontitis, and in rare individuals the periodontitis is mild and of late onset.<sup>7</sup>

Nail changes are apparent in advanced cases manifested by transverse grooving and fissuring.<sup>11</sup>

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.<sup>11</sup> Pyogenic liver abscess is increasingly recognized as a complication of PLS associated with impairment of immune system.<sup>12</sup>

The PLS locus has been mapped to chromosome 11q14-q21 with mutation of cathepsin C gene.<sup>13</sup> An interesting feature of cathepsin-C gene is that mutations in this gene also result in two other closely related conditions: the Haim-Munk syndrome (onychogryphosis, arachnodactyly, acral osteolysis, and pes planus) and prepubertal periodontitis (no PPK seen).<sup>14</sup> A common clinical manifestation in all three syndromes is severe early-onset periodontitis.<sup>14</sup> 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.<sup>15</sup> All PLS patients are homozygous for the same cathepsin-C mutations inherited from a common ancestor. Parents and siblings, heterozygous for cathepsin C mutations do not show either the palmoplantar hyperkeratosis or severe early onset periodontitis characteristic of PLS.<sup>9</sup>

A multidisciplinary approach is important for the care of patients with PLS. The skin manifestations of PPK are usually treated with emollients.<sup>8</sup> 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.<sup>12</sup> Etretnate, acitretin, and isotretinoin modulate the course of cutaneous lesions and periodontitis and preserve the teeth, if started during eruption of permanent teeth.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: Not required*

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DOI: 10.5455/2349-3933.ijam20141101

**Cite this article as:** Dhillon KS, Sharma D, Singh T, Srivastava R, Yadav S, Agarwal V, Khan A, Srivastava S. Spectrum of Papillon-Lefèvre syndrome. *Int J Adv Med* 2014;1:269-72.