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Review Article

Papillon-Lefèvre Syndrome: Prevalence and Characteristics in the Kingdom of Saudi Arabia

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Abstract

Objectives: The aim of the present review is to determine the prevalence and manifestations of reported cases of Papillon-Lefèvre Syndrome (PLS) in Saudi Arabia.

Methods: Pubmed and MEDLINE. Were combed through for relevant data includes any cases reported and published in Saudi Arabia were collected. Review of the associated factors and clinical manifestations of the reported cases of Papillon-Lefèvre Syndrome (PLS) were determined.

Results: The Papillon-Lefèvre Syndrome (PLS) is seen not uncommon with its prevalence rate in KSA. Age ranged from 3 - 19 years old with a mean of 10.33 years. Male constitutes 66.7% of the sample. The diagnosis of oral manifestations is challengeable and periodontal disease may represent mild form associated with cathepsin C gene mutation and allelic variations.

Conclusion: Although it is considered very rare syndrome, the number of reported cases in Saudi Arabia is not uncommon and this highlight the need for all dental health care providers to emphasize on its diagnostic and treatment modalities in the regional dental schools and clinical practice to establish a precise and definitive diagnosis and enhance the dental care services provided towards this group of patients.

Keywords: *Papillon-Lefèvre Syndrome; Prevalence; Oral Manifestation; Oral Health*

Abbreviations

PLS: Papillon-Lefèvre Syndrome; CTSC: Cathepsin C; A.a: *Actinobacillus actinomycetemcomitans*

Introduction

Papillon-Lefèvre syndrome (PLS) was first described in France by Papillon and Lefèvre in 1924 [1,2]. It is an autosomal-recessive disorder characterized by palmoplantar hyperkeratosis and aggressive periodontal disease, caused by a mutation in the cathepsin C (CTSC) gene [1]. The estimated prevalence is 1 to 4 cases per million [3]. The PLS has more incidence in Saudi Arabia and in Arabs generally than in other countries due to a higher rate of consanguineous marriages since consanguinity was reported in one-third of the cases [1,2,4]. There is no sex and racial predominance [2]. The onset of the disease starts with the eruption of primary dentition. Next, the gingiva becomes inflamed, leading to premature loss of the primary teeth. The gingiva resumes its normal state. Then, the cycle repeats itself when the permanent dentition erupts [2]. Eventually, the patient becomes edentulous by 15 [5]. The onset of cutaneous lesion usually starts at birth, or 1 to 2 months after, and commonly occurs between 6 months and four years [2].

Pathogenesis and aetiology

The aetiology and pathogenesis are still not fully understood. However, genetic, immunologic, and microbiologic factors have been attributed to PLS development [3]. PLS is caused by a mutation in the CTSC gene located on chromosome 11ql4-q21 [3]. Cathepsin C gene encodes the enzyme lysosomal cysteine protease; this enzyme is involved in the activation process of many immune cells such as polymorphonuclear leukocytes, macrophages, and its precursor. Thus, a mutation in the Cathepsin C gene leads to a deficiency of this enzyme. Moreover, the Cathepsin C gene is expressed in the epithelial regions affected by PLS, such as palms, knees, soles, and keratinized gingiva [2,3].

The decreased host defence mechanism increased liability to various infections, and the aggressive form of periodontitis in PLS patients are all owing to the mutation of the CTSC gene. Since the CTSC gene is involved in the activation process and expressed in several immune and inflammatory cells. Therefore, decreased activity of lymphocytes, polymorphonuclear leukocytes, and monocytes leads to the impaired immune system seen in PLS patients [1,2].

Gram-negative bacteria proved to be a primary factor in developing periodontitis, including PLS-associated periodontitis. The microscopic and cultural studies in PLS patients have found that the predominant bacteria are *Actinobacillus actinomycetemcomitans* (A.a). A.a was shown to represent nearly more than 50% of the total colony-forming units. Also, it was revealed that there is reduced neutrophils response to A. and *Staphylococcus* spp. Moreover, a high number of *Porphyromonas gingivalis, Prevotella intermedia*, *Prevotella loescheii, Bacteroides gracilis, Capnocytophagas* spp., and *Spirochetes* were also identified [1-3].

Clinical features

Associated features to the oral and dermatological manifestations discussed below are as follows: calcification of the falx cerebri and choroid plexus, mental retardation, hyperhidrosis (bromhidrosis) particularly of the hands and feet, nail dystrophy, and increased susceptibility to various infections ranging from mild skin infections such as furunculosis or pyodermas to severe ones as infections of liver, lung, and kidney [1,2,6,7]. Moreover, there are very few cases reported of patients with PLS having albinism [8-11]. The main explanation for this is that the genes responsible for these two rare conditions occur close to each other on the same chromosome [9].

Both dentitions erupt in normal sequence, at the normal age, with normal structure and form. However, signs of root resorption, microdontia, and incomplete root formation have been reported in some cases [1]. The oral lesions manifest when the primary teeth erupt. Once they erupt, the surrounding gingiva becomes inflamed, red, swollen, sore, and bleeds easily. After that, pathological periodontal pockets formed in which pus exudate is expressed under the slightest pressure. Brushing is difficult due to sore, painful gingiva, and mastication is painful due to the hypermobile teeth. Oral malodor and tender regional lymph nodes are also present. The pathognomonic oral signs of PLS are gingival abscess, heavy plaque accumulation, hypermobility, drifting and migration of teeth, and severe alveolar bone resorption. Eventually, all primary teeth are lost or extracted by the age of 4 or 5 years. Subsequently, the gingiva resumes its healthy natural

state. However, when the permanent teeth erupt, the cycle repeats itself, leading the patient to become completely edentulous during the teenage years. A panoramic radiograph reveals severe alveolar bone loss giving the teeth the "floating-in-air" appearance [1,3]. Patients with PLS have reduced vertical dimension of occlusion and senile facial appearance due to edentulism [1].

Cutaneous lesions start early at birth or 1 - 2 months of age. However, it commonly coincides with the oral lesions between 6 months and four years, which coincide with the eruption of primary teeth. The skin lesions develop in pressure areas, such as palms, soles, elbows, knees, knuckles, and ankles, with the most severely affected area are the soles. Less frequently affected areas are toes, legs, thighs, and rarely the trunk [2,3]. Also, it may extend to involve the thenar and hypothenar of palms, Achilles tendon, and external malleoli of feet [1]. The skin lesions vary in texture, color, and manifestation. They could be manifested as diffused or well-demarcated, dry, rough, thick, cracked, crusted, fissured, scaly, plaques or patches, which may be superimposed with infection. They could be white, light yellow, red, or brown, and erythema always precedes hyperkeratosis [1-3]. Skin lesions are worsened by cold weather, and the patient may experience pain during walking [1].

Clinical similarity of PLS to psoriasis

Several cases of patients with PLS were first misdiagnosed as psoriasis [12-15]. For example, a case of a 14-year-old girl who had a premature loss of her primary teeth at the age of 3. Skin manifestations become evident at 6 with loss of some permanent anterior teeth. However, a dermatologist treated palmoplantar keratoderma as psoriasis, which was slightly relieved [12]. A cohort study done on 47 patients with PLS reported that there were 2 cases suspected clinically to have psoriasis. They had extensive psoriasiform plaques in the scalp, trunk, and extremities, with severe nail dystrophy [13]. Another case of a 4-year-old Indian girl complains of loosening of teeth and discomfort during eating. The family reported that the skin lesion was first manifested when she was one year old. The skin lesions were diagnosed and treated as psoriasis with no improvement [15]. Thus, improper history, clinical and radiographic examination, and overlooking of dental changes that occur in patients with PLS may lead to misdiagnosing it as another disease or syndrome.

Differential diagnoses

The differential diagnoses of PLS include Haim-Munk syndrome, which is an allelic variant of PLS. It is also manifested with the palmoplantar hyperkeratosis and early onset of periodontal disease [2,3]. However, it presents with other symptoms such as arachnodactyly, acroosteolysis, pes planus, and nail deformities, which differentiate it from PLS [16]. In addition, acquired keratosis seen in psoriasis, tylotic eczema, lichen planus, hyperkeratotic tinea, paraneoplastic dermatosis, etc. may be considered a differential diagnosis of PLS. Still, it could be easily differentiated by the lack of aggressive periodontal destruction seen in PLS [17]. Other conditions are acrodynia, hypophosphatasia, cyclic neutropenia, severe congenital neutropenia, histiocytosis X, Takahara syndrome, Unna Thost syndrome, Mal de Meleda, Howel-Evans syndrome, epidermolytic palmoplantar keratoderma (Vörner's syndrome), keratoderma hereditarium mutilans (Vohwinkel's syndrome), and Greither's syndrome [1,3]. Regarding the radiographic findings, the differential diagnoses can include Chediak-Higashi syndrome and juvenile periodontitis [2].

Laboratory tests and diagnostic methods

Most children with PLS are of moderate size and have normal physical and intellectual development levels. Taking a family and medical history is the first step towards diagnosing PLS [3]. Patients with PLS have characteristic oral and skin changes. However, it may be necessary to conduct the following tests to confirm the diagnosis: hematological, hormone assay, height, and weight calculation, alkaline phosphatase, creatinine, glucose, cholesterol, triglycerides, electrolytes, total protein, conventional polymerase chain reaction for microbiological analysis, liver and renal function tests-moreover, other specific blood tests for immunoglobulin A, IgG, and IgM and lymphocyte antigen receptors. Additionally, radiological investigations include orthopantomography, intraoral periapical radiographs, lateral cephalogram, and abdominal and pelvic ultrasound. Although these tests in patients with PLS are usually within normal limits, they can still

distinguish this syndrome from other conditions [1,3]. Lundgren has observed that patients with PLS produced significantly less saliva and had lower buffer capacities than control subjects [18]. Also, neutrophil function test exhibit altered chemotaxis and phagocytic functions in biochemical analysis. Moreover, Urine analysis can be used for determining whether the suspected child has CTSC activity shortly after birth. Confirming the diagnosis can be done by molecular genetic test detecting deficiency or absence in CTSC enzyme activity [3].

Histopathological examination is nonspecific. However, a gingival biopsy may reveal parakeratosis, acanthosis, and hypergranulosis. The underlying connective tissue shows increased vascularity, and mixed inflammatory cell infiltrate. Skin biopsy shows a thick layer of hyperkeratosis, hypergranulosis, acanthosis, and irregular rete ridges of the epidermis. Perivascular mononuclear infiltration is seen in papillary dermis [1,3].

Treatment

Treating patients with PLS is challenging and needs a multidisciplinary approach and requires parents and patient cooperation for a successful outcome. The main goal is to remove the causative organisms to stop the rapid periodontal destruction, reduce hyperkeratotic skin lesions and relieve the pain [3]. The Dental treatment includes oral hygiene instructions, scaling and root planning, chlorhexidine gluconate mouth wash, and systemic antibiotics. Hattab mentioned in his review that there are several studies that reported different successful treatment outcomes regarding the use of various antibiotics such as tetracycline, amoxicillin-clavulanic acid, amoxicillin and metronidazole, and metronidazole [3]. Extraction of hopeless primary teeth provides a better environment for permanent teeth eruption [1,3]. In both dentitions, extraction of a mobile hopeless tooth should be done under antibiotic coverage due to the impaired immune system. For permanent dentition, prophylaxis, scaling, and root planning should be done every 2-3 months. Moreover, for moderately mobile teeth splinting is necessary [3].

The prosthetic challenges posed by severely atrophic thin alveolar ridges have been known to clinicians for many years. There has been some research reporting the use of implants in patients with severe periodontitis, and the results indicate that implants can provide a successful treatment for patients with periodontitis [2]. Removable complete or partial dentures can be used as part of a traditional oral rehabilitation for patients with PLS. It is usually considered interim treatment to improve their ability to eat, enhance their aesthetics and self-esteem. Regarding Implant-supported prostheses, oral rehabilitation with implants is a viable treatment option for patients with PLS. It provides better support, retention, and stability [19]. Ellegaard mentioned in his study that implant therapy has been reported as successful for patients with PLS. Researchers have reported periodontally compromised as well as periodontally healthy individuals can get the most benefit from dental implants [20]. A systematic review done by Nassani., *et al*. reported that dental implants have an 84% survival rate among PLS patients. Studies conducted on individuals with progressive periodontitis found that follow-up visits, oral hygiene routines, and the stage of periodontitis influence the survival rate of dental implants [21]. However, dental rehabilitation is the main encountered problem for the early edentulous patients with bone deficiency for implantation or prosthesis.

The Dermatological treatment is mainly based on lubricants, using keratolytic agents with salicylic acid, lactic acid, or urea in a neutral base [3]. Also, the use of topical anti-inflammatory steroids and systemic antibiotics was reported in case of inflammation [3]. In addition, the use of topical and systemic retinoids has beneficial effect [1,3].

Discussion

Papillon-Lefèvre Syndrome (PLS) is a Congenital defect in cathepsin C, causing palmoplantar hyperkeratosis, juvenile periodontitis, which affects both dentitions, and immunodeficiency. Approximately same signs and symptoms of skin and periodontal conditions were present in Saudi Arabia as reported in the literature surveyed and Age range reported in KSA is in line with the worldwide age groups affected. Males were more frequently affected than females. The PLS seen in our region in the dental clinic at the teenager's group and not at the earliest stage of the disease recognition and so the condition of the dentition is usually hopeless and most reported cases was undergoing extraction and rehabilitation with different prosthetic removable and supported fixed prosthesis [2].

Authors	Ethnicity\ Nationality	Age	Sex	Signs and symptoms	Treatment
Abdullah Al Farraj AlDosari	Saudi	19-year-old	F	- Patient diagnosed with PLS was referred to the prosthodontist. - She reported with grade III mobility of all teeth except the second molars. She was diagnosed with severe periodontitis with generalized bone loss in the upper and lower jaw.	- Extract all the teeth except for the second molars of both upper and lower arches. - Implant-supported fixed prostheses
Hytham N Fageeh	Yemeni	11-year-old	M	- Patient complains from mobile teeth for the last 6 months. - Physical examination shows: Bilateral hyperkeratotic lesions on the palms and soles. - Intraoral examination had shown the presence of permanent maxillary right canine, first and second premolar, first molar, permanent maxillary left lateral incisor, canine, first and second premolar, and first molar. In mandible, permanent mandibular right central incisor, canine, first premolar, first molar, left central incisor, canine, second premolar, and first molar were present. All other permanent teeth were missing. Of these remaining teeth, many were showing varying degrees of flaring mobility. Furthermore, severe gingival inflammation associated with thick plaque accumulation and deep periodontal pockets was present - On radiographic examination, alveolar bone loss associated with all the affected teeth was noted. Also, third molar buds were present in their bony crypts except for the lower left third molar, with normal crown development and no associated bony changes.	The treatment plan included oral hygiene modification, nonsurgical periodontal therapy, extraction of all the remaining mobile teeth, and insertion of maxillary and mandibular dentures

Hytham N Fageeh	Yemeni	12-year-old	M	- Patient complains from mobile teeth for the last 6 months. - Physical examination shows: Bilateral hyperkeratotic lesions on the palms and soles. - I\O examination shows: presence of permanent maxillary right lateral incisor, canine, first premolar, first molar, permanent maxillary left canine, second premolar, and first molar. In mandible, permanent mandibular right central incisor, lateral incisor, canine, first premolar, first and second molars, left central incisor, canine, first and second premolar, and first molar were present. All other permanent teeth were missing. - Of these teeth, maxillary right first molar, left second premolar, first molar, mandibular right canine, first premolar, and first molar were showing varying degrees of flaring and mobility. Severe gingival inflammation associated with thick plaque accumulation and deep periodontal pockets was present. - On radiographic examination, alveolar bone loss associated with all the affected teeth was noted. Also, third molar buds were present in their bony crypts, with normal crown development and no associated bony changes	The treatment plan included oral hygiene modification, nonsurgical periodontal therapy, extraction of all the remaining mobile teeth, and insertion of maxillary and mandibular dentures. Consideration of dental implants will be considered after the age of 18.

Aiman Shawli, Yazan Almaghrab, Abdullah S. AlQuhaibi, Yousef Alghamdi, Abdulbari M. Aboud.	Saudi	7-year-old	M	- He first presented to the dermatology clinic when he was five years old complaining of dry scaly patches on the skin. The patient's medical history revealed that it started at the age of four months in the form of desquamation and erythema on the hand and feet, sparing the trunk, back, and face. - He was found to have erythematous hyperkeratotic skin plaques and papules with scales over the planter and palmar aspect of both hands with similar lesions observed on both feet, legs, scalp, and ears with nail pitting - He has dental caries and delayed teething	
Shiv Shanker Pareek, Abdul Karim Al-Aska.	Saudi	I7-year-oId (Patient 1)	F	- Patient presented with well demarcated erythematous, hyperkeratotic, and scaly lesions on the palms and soles. Gradually the condition spread to the knee and elbow. - Diffuse engorgement of gingiva and fetid odor were noticed at the age of 3 years. - Physical examination revealed fissuring of the nail was present. Cutaneous changes such as well demonstrated erythematous, hyperkeratotic scaly lesions with fissuring were noticed on the palms and soles. Skin lesions disappeared on the knees and elbows without any marks at the age of 9. Oral examination showed inflamed marginal gingivitis and deep periodontal pocket formation.	

Shiv Shanker Pareek, Abdul Karim Al-Aska.	Saudi	I6-year-oId (Patient 2)	M	- Patient exhibiting premature loss of teeth and white thick patches on the knees, elbows, palms, and soles oi the feet since early childhood. - On examination, white hyperkeratotic lesions were present on the knees and elbows, dorsal aspects oi the hands and soles of the feet. The knuckles of the hand were also affected, and multiple warty growths were present on both hands. - Intra-oral examination showed the presence of six teeth. The surrounding gingiva was slightly edematous and inflamed.	
Shiv Shanker Pareek, Abdul Karim Al-Aska.	Saudi	I5-year-oId (Patient 3)	F	- Patient having well demarcated, erythematous, hyperkeratotic, and scaly lesions on the palms and soles. Diffuse engorgement of gingiva and a fetid odor - Cutaneous changes and oral presentation were similar to those of Patient 1.	
Shiv Shanker Pareek, Abdul Karim Al-Aska.	Saudi	6-year-oId (Patient 4)	M	- Patient presented with fully demarcated, erythematous, hyperkeratotic, and scaly lesions on the palms and knees (Fig. 1) and soles since he was 1 and a half years old. Cutaneous manifestations were remarkably prominent under cold conditions. - The deciduous teeth started to loosen at the age of 3, and most of them fell out by the age of 4. - Skin and orodental examination was similar to that of Patient 2	

Shiv Shanker Pareek, Abdul Karim Al-Aska.	Saudi	5-year-oId (Patient 5)	M	- Patient reported to the clinic with red, erythematous, hyperkeratotic, and scaly lesions with cracks and fissures on the palms and soles since the age of 1. Gradually, the condition had spread to his knees. - Both upper central incisors had fallen out. Remaining deciduous. teeth were intact but had started to loosen.	
Shiv Shanker Pareek, Abdul Karim Al-Aska.	Saudi	3-year-oId (Patient 6)	F	- Red, erythematous, scaly, - Hyperkeratotic lesions on the soles of her feet,	
Zyad M. AIBarrak, Adel S. Alqarni, Elna P. Chalisserry, Sukumaran Anil.	Arab	3-year-old	F	- All her anterior and most of her posterior primary teeth were lost. - There was inflammation of her gingiva with plaque accumulation in her teeth - thickening of the skin was observed in her knees, elbows, and toes. - Basic Periodontal Examination (BPE) using World Health Organization (WHO) 621 probe showed a code 4 in her remaining teeth.	- Scaling. - her parents were advised to maintain her oral hygiene. Home care measures were emphasized. - Temporary space maintainers were fabricated and peri- odic follow up was advised.
Zyad M. AIBarrak, Adel S. Alqarni, Elna P. Chalisserry, Sukumaran Anil.	Arab	4-year-old	M	- Exfoliated maxillary right central and lateral incisor. - Gingivitis and plaque accumulation were present in his remaining teeth. - The BPE showed a code between 3 and 4 in his remaining teeth. - There was alveolar bone destruction around all erupted and erupting dentition. - Keratosis of his palms and soles was present at a mild degree	- Scaling - We advised that he had periodic oral hygiene measures. - A temporary denture was fabricated to wear during the daytime.

Zyad M. AIBarrak, Adel S. Alqarni, Elna P. Chalisserry, Sukumaran Anil.	Arab	11-year-old	M	- Mobile protruded and migrated maxillary and mandibular anterior teeth - All his primary teeth were lost. There was severe bone destruction around his permanent teeth. His molars were all mobile with less than one third bone support. - A BPE code 4 was recorded in all his molars and incisors. - There was bleeding from his gin- giva with halitosis - He had dermatologic manifestations such as keratinized skin in his joints, palms, and soles.	- Scaling - Periodic scaling (monthly) was advised and strict oral care measures were advised.
Zyad M. AIBarrak, Adel S. Alqarni, Elna P. Chalisserry, Sukumaran Anil.	Arab	12-year-old	M	- Multiple exfoliated teeth. - Gingival enlargement around erupting teeth. - Most of his permanent anterior teeth were lost with severe bone destruction around his remaining teeth. - A periodontal examination recorded a score of 4 (deep pocket) in his molars and incisors. His lower molars appeared floating without any bone support. - There was severe palmar plantar keratosis with keratinization of the dorsal surface of his hands. His molars were extracted.	- Transitional dentures were given - A follow- up regimen was advised.

Zyad M. AlBarrak, Adel S. Alqarni, Elna P. Chalisserry, Sukumaran Anil.	Arab	14-year-old	M	- Intraoral appearance with loss of permanent anterior from both jaws, severe inflammation, and enlargement of the gingiva. - On radiographic examination severe bone destruction was noticed around his remaining teeth. - Periodontal recording using the BPE index showed a score of 4 for most of his remaining teeth. - Associated dermatologic findings were conclusive of PLS, such as severe palmar plantar keratosis which affected the dorsal surface of his palms.	- Scaling and root planning - He was kept on a strict oral hygiene regimen. - A temporary partial denture was fabricated, and he was scheduled for implant therapy at a later stage.

Table 1: *Summary of characteristics of included PLS cases in Saudi Arabia.*

Year	Author	Residence (national or ethnic origin)	Consanguinity	Age	Sex	Age at onset of		Chief complains	Treatment
2015	Somia Iqtadar [22]	Pakistani	Yes	16 years	Male			High-grade fever of 2 months duration.	Broad-spectrum antibiotics, antipyretics, multivitamins, topical steroids, and topical keratolytics.
2006	Atsushi Ikeshima [23]	Japanese		7 years	Female	Since 2004		Deciduous tooth mobility	The residual deciduous teeth were extracted on 23rd April 2005, and the patient is currently receiving treatment and follow-up care.
1986	Preus H and Gjermo P [24]		No	5 years	Female	At age 3 years	1 1/2 - 2 years	An aggressive periodontitis.	

1986	Preus H and Gjermo P [24]			2 years					
2005	Christopher J. Lux [25]			7 years and 9 months	Male			Hyperkeratosis of the palms and soles as well as advanced periodontal disease affecting all erupted permanent teeth.	Mechanical and antibiotic periodontal treatment and orthodontic treatment
1979	E. Haneke [17]		No	7 years	Female	1 1/2 years			Keratolytic treatment for skin lesion Consistent oral hygiene and prophylaxis against infections were carried out
2013	Anupriya Sharma [26]		Yes	16 years	Male	6 months	3 years	Loose teeth and markedly inflamed gingiva, with excessive bleeding and severe halitosis	Periodontal treatment+ 0.12% Chlorhexidine mouth rinse + systemic antibiotic and finally a removable denture
2013	Anupriya Sharma [26]		Yes	11 years "Younger sibling to the previous patient"	Female			Severe gingival inflammation, abscess formation, and deep periodontal pockets	
2012	Fayiza Yaqoob Khan [27]		Yes	11 years	Female			Loose teeth and discomfort in chewing along with recurrently swollen and friable gums.	
2012	Fayiza Yaqoob Khan [27]		Yes	13 years "Elder sister to previous patient"	Female			Loose teeth and discomfort in chewing along with recurrently swollen and friable gums.	

2006	Schacher B [28]	Eritrean origin	No	3 years	Male	One month			Combined mechanic and antibiotic periodontal therapy, systemic AB OHI
2006	Schacher B [28]	Eritrean origin	No	5 years	Male	One month			Combined mechanic and antibiotic periodontal therapy, systemic AB OHI
2021	Yasmin Mohamed Yousry [29]	Egyptian	No	4 years	Male			Premature loss of anterior teeth, friable and bleeding gums and swelling related to the upper anterior region.	Conventional periodontal treatment, chlorhexidine gluconate MW and systemic ABs
2015	Sunil Kumar Biraggari [30]		Yes	13 years	Female	4 years		Loose upper front teeth along with bleeding gums in the last 2 years.	Conventional periodontal therapy, Systemic Abs, OHI, Chlorhexidine mouth rinse, surgical periodontal therapy, and oral retinoids for skin lesion
2013	Margi V. Bhavsar [31]	Indian	No	14 years	Female	3-4 years	4-5 years	Premature loss of deciduous and permanent teeth and mobility in remaining teeth.	Conventional periodontal therapy, Systemic Abs, OHI, Chlorhexidine mouth rinse, surgical periodontal therapy, partial denture and oral retinoids for skin lesion
2013	Margi V. Bhavsar [31]	Indian	No	6 years "sister of the previous pt"	Female			Mobility in relation with some of her deciduous teeth and then early exfoliation of same.	Conventional periodontal therapy, Systemic Abs, OHI, Chlorhexidine mouth rinse, surgical periodontal therapy, partial denture and oral retinoids for skin lesion

2012	Shabina Sachdeva [32]			15 years	Male		3 years	Lost most of his teeth and i ability to chew with the remaining 'loose' teeth.	Extraction of remaining teeth due to poor prognosis and complete denture construction. Referral to dermatology department for skin lesion
2014	Aasim Farooq Shah [33]	indian	Yes	28 years	Female		3-4 years	Premature loss of permanent dentition.	Fabrication of full dentures.
2014	Aasim Farooq Shah [33]	Indian	Yes	16 years "brother of previous pt"	Male			Esthetic problems and difficulty eating for 1 year due to the loss of permanent teeth.	Fabrication of dentures for resorbed alveolar areas.
2019	Lashika V Tambe [34]		Yes	12 years	Male		10 years	Early loss of deciduous teeth, mobility of teeth and sensitivity of teeth on drinking cold water.	Referral to a Dermatologist for skin lesions. The dental treatment included aggressive form of periodontitis managed by the Periodontist.
2009	Mashkoor Ahmad [35]		Yes	15 years	Male			Persistent thickening and scaling of skin of palms and soles, which worsened during winter season.	
2020	Aiman Shawli [14]			7 years	Male	4 months		Dry scaly patches on the skin.	Calcipotriol cream and moisturizing cream. Acitretin capsules and a skin punch biopsy. Referral to pediatric genetics and dental services.

2013	Ramesh Krishnan [15]		Yes	4 years	Female	One year		Loose teeth and discomfort while eating.	Conventional periodontal ttt and medication.

Table 2: *Summary of characteristics of PLS reported cases (regional area).*

Periodontal disease occurs with the early loss of deciduous teeth, followed by the loss of permanent teeth during adolescence. Prosthodontics management of PLS patients is very complex and it may require invasive therapeutic treatments. Early diagnosis is essential for achieving good results during treatment management avoiding the possibility that patients are early edentulous. The Severity of periodontal disease is amplified in the presence of ACC and the background of Papillon-Lefèvre Syndrome (PLS) in contrast with other syndromes like Ehlers-Danlos syndrome, The patient's problems usually involve the presence of an abnormal collagen. This protein is the main component of connective tissues. Additionally, Kindler syndrome represents a heterogeneous group of inherited blistering mucocutaneous disorders. Symptoms of Kindler syndrome in the mouth are mild, with tenderness and erythema of the gingiva. Buccal vestibule depth may be reduced, and gingival recession may occur [36].

The proliferation of cutaneous keratinocytes is uncommon in psoriasis, unlike other chronic skin diseases. Despite the fact that oral lesions may occur in psoriasis patients, these lesions are distinctly uncommon, because they can range from white plaques to red plaques to ulcerations. An accurate diagnosis of intraoral psoriasis is difficult, compared to palmoplantar keratosis manifestations of Papillon-Lefèvre syndrome, the skin semblance is more severe, and the periodontal disease is milder and exhibiting cathepsin C gene mutations and representing allelic variants of the mutated gene responsible for Papillon-Lefèvre syndrome [29].

Papillon-Lefèvre syndrome is a rare genetic disorder that can cause severe dental abnormalities and skin and nail changes. It is usually characterized by the destruction of the terminal phalanges of the hands and feet, resulting in a characteristic claw-like appearance. Skin lesions associated with the disorder are usually painful, red and inflamed, and can be seen on the palms of the hands and soles of the feet [1]. In comparison, skin lesions associated with psoriasis are usually red and scaly and can appear anywhere on the body. While both conditions can cause inflammation and pain, the skin lesions associated with Papillon-Lefèvre syndrome are often more severe and can lead to infection or tissue destruction if left untreated. Treatment for both conditions is typically aimed at relieving symptoms and preventing further damage to the skin [35].

As a result of Papillon-Lefèvre syndrome, the gingiva becomes thickened and discoloured, and teeth and jawbone are rapidly destroyed. Symptoms of psoriasis that affect the mouth can range from dry mouth to swollen gums to ulcers. In Papillon-Lefèvre syndrome, medication is usually administered to relieve symptoms and prevent further damage to the teeth and jawbone, whereas in psoriasis, oral medications are prescribed like antiseptic mouth rinses [35].

The Haim-Munk syndrome is a rare genetic disorder that is characterized by various physical abnormalities, such as facial dysmorphism, hearing loss, and intellectual disability. Oral lesions associated with this disorder can include thickening of the hard palate, small teeth, and gingival hyperplasia [37]. In Haim-Munk syndrome, the skin lesions are seen on the face, scalp, palms, and soles as round or oval patches of yellow brown to black scaly skin. The treatment for Haim-Munk syndrome may involve hearing aids, physical therapy, and speech therapy [38].

As aforementioned, the etiopathogenesis of the syndrome is relatively obscure and immunologic, genetic, or possible bacterial aetiologies have been proposed [36]. A possible bacterial aetiology has also been proposed hence treatment modalities including administra-

tion of variety of antibacterial medications should be considered [39]. However, such use of antibacterial medications should be closely monitored as prolonged administration might represent related-adverse side effects. Also, the associated involvement of periodontal diseases may lead to progressed bony destruction that results in atrophic lesions in maxilla-facial region hence the therapeutic approach for patients with PLS is most of the times challenging and need comprehensive rehabilitation when considering both the aesthetic and functional aspects of dental treatment.

Conclusion

This review emphasizes on the importance of the early diagnosis of the non-dental signs and symptoms of the PLS disease in order to aid patients saving their teeth and lessen the concurrent complications. A multidisciplinary is the key element for management of patients with PLS thus increase the awareness of PLS and its related clinical manifestations, involvement of oral and dermal conditions among dental health care providers is needed.

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Conflicts of Interest

The authors declare that there are no conflicts of interests.

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