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Papillon-Lefèvre Syndrome - A Case Report and a Multidisciplinary approach in the Treatment of 18 Years Old Sudanese Female

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Abstract An eighteen years old Sudanese female patient presented with keratotic plaques over the skin of her palms and soles and swollen gums since the age of 4 years with the subsequent loss of most of her primary and permanent dentition. These findings are consistent with Papillon-Lefèvre syndrome. Papillon-Lefevre syndrome is a rare autosomal recessive genetic disorder with a clinical presentation which includes palmer planter keratoderma associated with the precocious progressive periodontal disease that results in early exfoliation of both the primary and permanent dentitions.

Keywords Papillon–Lefèvre syndrome (PLS), Palmar-plantar keratoderma, Periodontitis, Premature teeth loss

1. Introduction

Papillon-Lefèvre syndrome (PLS) or palmoplantaris keratoderma with periodontopathia is an inherited autosomal recessive genodermal trait, affecting children characterized by diffuse, transgradient palmoplantar keratoderma (PPK), progressive destructive periodontitis starting in early childhood, between the ages 1-4 years, premature loss of primary teeth and recurrent [1]. It has a prevalence of 1-4 cases per million persons [2]. There are no racial predominance or gender predilection equally affecting both males and females [3].

Further symptoms and findings may comprise of recurrent cutaneous and systemic pyogenic illnesses, nail dystrophy and hyperhidrosis [4]. Van Dyke et al. reported that the patients classically have a major disease associated with quantitative neutrophil abnormalities and almost of the afflicted patients are immunocompromised [5]. Pyogenic liver abscess is an unusual presentation of the disease. However, PLS patients appear to be exceptionally susceptible to acquire pyogenic liver abscess [6].

2. Case Presentation

This case report illustrates a case of PLS classic clinical features and a review the pertinent literature. An eighteen-year-old female born to consanguineous parents was referred to the clinics at the Khartoum College of Medical Sciences (KCMS) with redness and peeling off of the skin of hands (Figure 1) and feet, cough, and pain of one-month duration. Her siblings and cousins did not have similar histories.

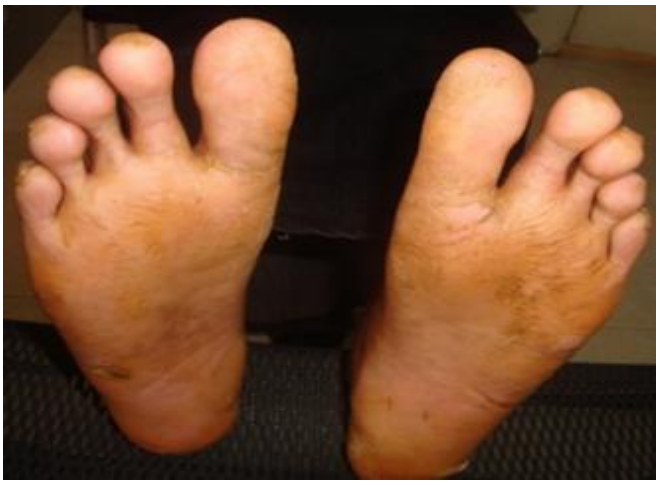

Figure 1. Diffuse plantar keratoderma both feet

The patient mentioned exacerbations and remissions of the skin lesions (Figure 1) and multiple infections since early childhood. She had a normal outcome at birth and had normal developmental landmarks till the age of three. During the 3rd year of her life, she started developing fissures in the skin of her palms and soles that caused the peeling off of the skin leaving thin red and shiny skin underneath; that is suggestive of keratoderma. She repeatedly contracted systemic infections. She had a cough for last one month that

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was initially dry and, later on, became productive. She used to get short periods of a cough which was diagnosed as pertussis.

The general physical examination showed a young lady of normal height and moderate physique with a steady gait. The blood pressure of the patient was 120/70 mmHg, a pulse rate of 116/minute, a temperature of 37.7°C and a respiratory rate of 20/minute. There was a slightly noticeable swelling in the thyroid region of the neck (Figures 2 and 3). The family history demonstrated there were no similar disorders in the family. Her physical and mental development were also normal.

Figure 2. Lateral view of the neck showing the enlarged thyroid gland

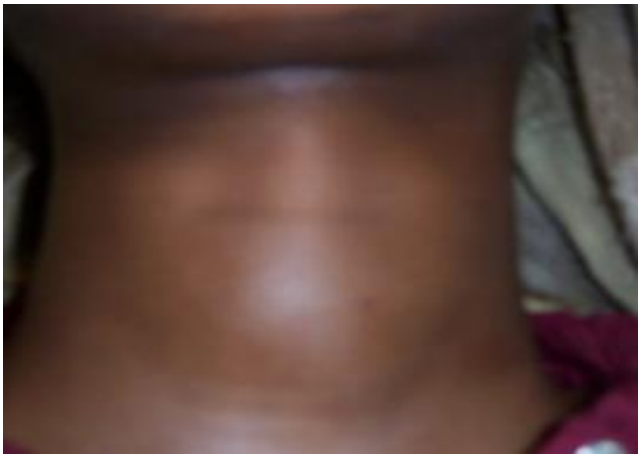

Figure 3. Frontal view of the neck showing the enlarged thyroid gland

The clinical oral examination revealed the absence of her upper incisors, upper and lower canines, upper and lower molars. A Miller's grade III mobility was seen on teeth number 14, 15, 24, 25, 23, 35 and 44 and was thus advised to extract these teeth. Her deciduous teeth started exfoliating at about the age of three years, and then her lower incisors erupted also become became mobile.

Routine hematological examination revealed a hemoglobin level of 10.0 g/dl, the total leucocyte count of 9200 and the ESR was 20 mm/hour. Urine analysis examination showed 15-20 pus cells and 3-4 red blood cells which are suggestive of urinary tract infection. The remainder of the biochemical investigations were within normal limits.

Based on history, clinical examination and investigations, and in consultation with the referring dermatologist a diagnosis of Papillon-Lefèvre syndrome was made.

A multidisciplinary treatment approach involving the dermatologist, periodontist, and prosthodontist was undertaken for the treatment of the patient. For the treatment of the dermatological condition, the administration of anti-inflammatory emollients and keratolytic agents, topical steroids and salicylic acid were very successful. Oral retinoids were also prescribed for the patient.

In considering the whole situation, it was mandatory to satisfy the esthetic and functional demands of the patient as a priority. Following the extraction of all the remaining hopeless teeth (Figures 4 and 5) as the early rehabilitation affords the patient to develop a normal social life, improved esthetic and function and facial support. Various treatment modalities for restoring the missing tooth were thought, and a complete removable denture was proposed and eventually undertaken.

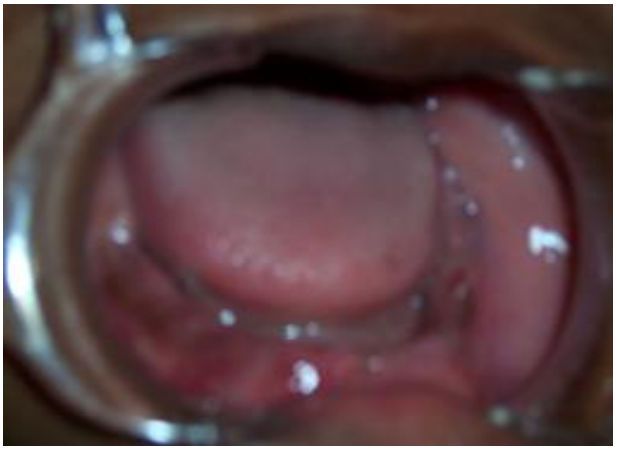

Figure 4. Intraoral picture of the lower jaw following the extraction of the "hopeless teeth"

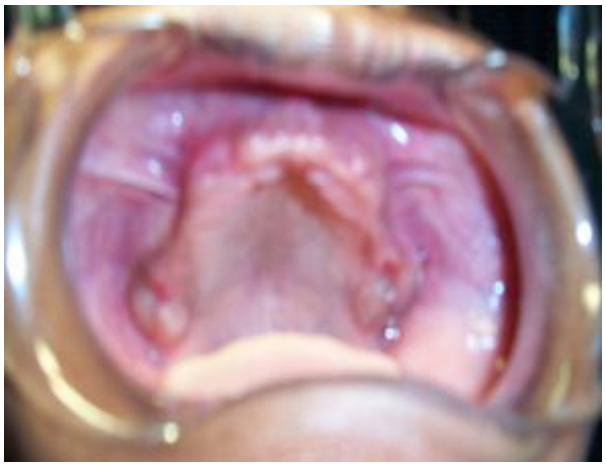

Figure 5. Intraoral picture of the upper jaw following the extraction of the "hopeless teeth"

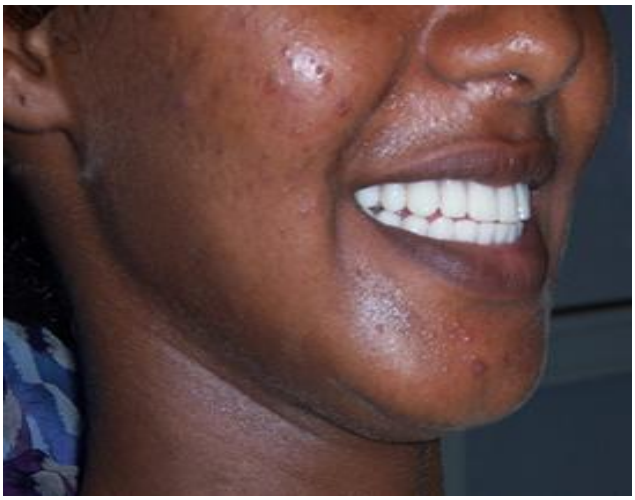

Figure 6. The right frontal lateral view of the face following the insertion of the denture

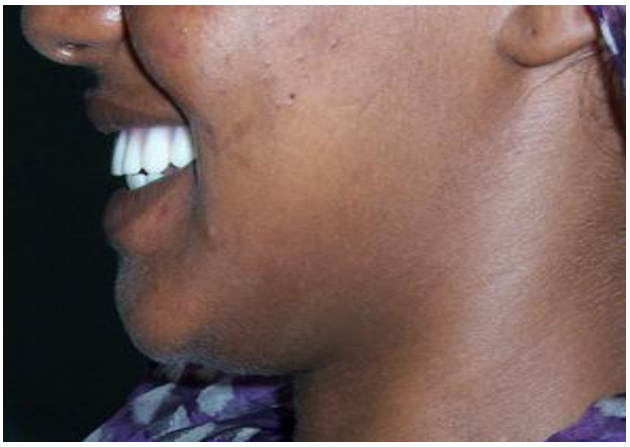

Figure 7. Left profile of the patient following the insertion of the denture

Primary impressions were made using irreversible hydrocolloid[1]. A set of special trays were made on the primary casts with double thickness wax spacer. The final impressions were made with a special tray using low viscosity silicone impression material[2]. The standard clinical protocol was followed during jaw relation procedure, and the casts were mounted on an articulator. Teeth arrangement was undertaken to provide a refreshing new smile. Denture try-in was completed, and dentures were fabricated in high impact heat polymerized acrylic resin. After finishing and polishing the dentures were inserted (Figures 6 and 7).

On delivery of the complete denture, the patient was informed in detail concerning the possible discomfort she might experience in first days due to the presence of the denture in her mouth. The patient was later recalled for post insertion checkups and necessary adjustments.

3. Discussion

Papillon-Lefèvre is a rare genodermal condition that was initially described in 1924 by two French Physicians Papillon and Lefèvre, in a brother and sister suffering from palmoplantar hyperkeratosis associated with severe periodontal destruction and premature loss of deciduous as well as permanent dentition [7]. In 1964 Gorlin et al. added a third component to the syndrome; the dural calcification [8].

There are no prevalence studies reported in Sudan. Nevertheless, there are two previous reports in the Sudan of similar conditions [9, 10]. Globally, a prevalence of 1-4 cases per million in the general population has been documented with a carrier frequency of 2-4 per thousand population with no sexual predilection [3, 4].

Papillon and Lefèvre syndrome (PLS) is characterized by palmoplantar keratoderma, psoriasiform plaques; that vary from mild psoriasiform scaly skin to overt hyperkeratosis of the elbows and knees. The periodontal disease with consequential premature loss of the primary and permanent teeth, and intracranial calcifications [11], which may occur focally, but more frequently they include the whole surface of the palms and soles [12]. The psoriasiform plaques usually occur within the first 2-3 years of life [13], which are often associated with hyperhidrosis of the soles and the palms producing a foul-smelling odor [2]. Siragusa et al. have reported that dermatological condition may worsen in winter and may be concomitant with painful fissures [14].

The deciduous teeth develop and erupt normally, however, these teeth are associated with concomitant gingivitis and ensuing periodontitis. The resulting periodontitis is characteristically refractory to conventional periodontal therapy modalities. Eventually, the deciduous dentition is usually prematurely exfoliated by the age of 4 years. Following the exfoliation, the gingivitis subsides, and the gingiva consequently appears healthy. However, the process of gingivitis and periodontitis is usually repeated with the eruption of the permanent dentition, and there is subsequent premature exfoliation of the permanent teeth as soon as they erupt though the third molars are occasionally spared [15, 16]. As of resorption of underlying alveolar bone as a result of the aggressive form of the periodontitis, the teeth appear as floating in the air in radiographs [17].

The pathogenesis of PLS remains controversial. The dermatological lesions are assumed to be due to the disorders in the ectodermal and mesodermal components. However, this does not explain the rapid loss of both the deciduous as well as permanent teeth in the order of their eruption [18].

There are three postulations suggested as being responsible for the initiation and progression of the syndrome. Firstly, the associated impairment of qualitative attributed the Polymorphonuclear lymphocytes (PMNL) accompanied by a decrease in cell migration has been noted. Secondly, the presence of numerous virulent gram-negative anaerobic pathogens (as Porphyromonas gingivalis, Capnocytophaga gingivalis, Aggregatibacter actinomycetemcomitans, Peptostreptococcus micros, Fusobacterium nucleatum, and spirochetes) in the periodontal plaques and periodontal pockets have been noted. These periodontopathogens are thought to act as trigger

1 Alginate, Cavex 37, Netherlands.

2 Heraeus Kulzer GmbH, Germany

factors. Thirdly, a defect of immune-mediated mechanisms including the reduced lymphocyte response to the periodontopathogens, depression of helper/suppressor T cells ratio, impaired monocytic function, elevation of serum IgG and the degenerative changes in the plasma cells have been identified [17, 19-22].

Genetic studies associate Papillon-Lefevre syndrome due to mutations in the cathepsin C (CTSC) gene mapped to chromosome 11q14-2 that codes for cathepsin C (dipeptidyl peptidase I). The CTSC gene is a lysosomal protease that takes part in the epidermal differentiation and desquamation and in the serine proteases activation that is found in cells of the immune system which include polymorphonuclear leukocytes, macrophages, and their precursors. A mutation in the CTSC gene has the total potential loss of cathepsin C activity and reduced activity in the obligate carriers results in the susceptibility to specific virulent pathogens which has been demonstrated in PLS patients [13, 23].

The cathepsin-C gene is seen in the epithelial regions of the palms, soles, knees, and the keratinized oral gingiva; regions that are usually affected by PLS. All PLS patients are homozygous for the same cathepsin-C mutations which are inherited from a common ancestor. The parents and the siblings, which are heterozygous for the cathepsin C mutations present neither the palmoplantar hyperkeratosis nor the severe aggressive periodontopathia which is characteristic of PLS [8].

The treatment of PLS patients is a multidisciplinary approach. The dermatological manifestations are usually treated with emollients [7]. Oral retinoids such as acitretin, etretinate, and isotretinoin have been reported to be useful for both the oral and dermatological lesions of PLS. The use of retinoid as treatment reduce the palmoplantar keratoderma and slow the alveolar bone lysis and may produce normal dental development if initiated during the eruption of the permanent teeth [24].

The periodontitis associated with PLS is usually difficult to control with conventional periodontal therapy modalities. Effective treatment of periodontitis includes extraction of the hopeless teeth combined with an appropriate oral antibiotic, the use of mouthwashes and professional scaling and root planing of the teeth, but usually, this procedure is not enough. Eventually, however, primary or remaining teeth are extracted and are replaced by either removable or fixed prosthetics [25].

The vitamin A (synthetic retinoids – etretinate, isotretinoin, and acitretin) have been reported to reduce the development of periodontitis and maintain the teeth. The antibiotic therapy should also be prescribed to reduce the active periodontitis, to maintain the teeth and to avoid the bacteremia, and the treatment of recurrent infections and pyogenic liver abscesses [26].

The observation of the thyroid enlargement in this patient is thought to be a potential association with the PLS. However, this from the western region of the Sudan which is a widely assumed endemic areas of iodine deficiency due to environmental and social factors.

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