CASE REPORT

Parental Consanguinity as a Risk Factor in Papillon-Lefevre Syndrome: A Case Report

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ABSTRACT

Papillon- Lefevre syndrome (PLS) is a very rare autosomal recessive disorder characterized by palmoplantar hyperkeratosis and severe early onset of destructive periodontitis leading to premature loss of both primary and permanent dentition.PLS is transmitted as an autosomal recessive condition and consanguinity of parents is evident in about one third of cases. Here we report a case of a 13 year old boy who referred to the Department of Dentistry, Sri Manakula Vinayagar medical college and hospital, Puducherry, India with the complaints of early loss of multiple teeth. He was a first child of healthy consanguineously married parents. On oral examination absence of maxillary and mandibular incisor teeth noted with generalized mobility of all remaining teeth. Hyperkeratosis on the skin of the palms and soles were found. Based on the patient history,clinical and radiographic findings a final diagnosis of PLS was made.

KEYWORDS: Consanguineous marriage, Papillon-Lefevre syndrome, Periodontitis

INTRODUCTION

Consanguineous marriage is the union of individuals having a common ancestor. Consanguineous marriages are associated with an increased risk for congenital malformations and autosomal recessive diseases. In 1924, two French physicians Papillon and Lefevre described a brother and sister with a condition characterized by diffuse palmoplantar keratoderma and precocious aggressively progressing periodontitis, and premature loss of primary and permanent teeth. The condition is presently referred as PLS.[1] PLS usually manifests itself between the ages of 6 months to 4 years, coinciding with the eruption of primary teeth. PLS affects both sexes equally with no racial predominance.[2, 3] PLS is estimated to have a frequency of 1-4 per million with a carrier rate of 2-4 per thousand.[4] Till date more than 300 cases of PLS have been reported worldwide.[5] The incidence of PLS is higher in Middle East countries and Arab communities than other parts of the world, and this may be related to consanguineous marriages. Etiopathogenesis of PLS is not fully understood, and various factors have been considered. The disorder can be hereditary, immunologic, or associated with microbial factors. The etiology of PLS appears to be genetic in most cases, characterized by mutation of the Cathepsin C gene (CTSC) on chromosome 11q14.1-q14.3.[6, 7, 8] PLS is autosomal recessive, and consanguinity has been reported in 20-40% of patients.[7] This article presents a brief overview of PLS and describes the clinical and radiographic presentation in a 13-year old boy with characteristic dental and dermatological features and its association with parental consanguinity.

CASE REPORT

A 13 year old boy (Figure 1)reported to the Department of Dentistry, Sri Manakula Vinayagar medical college and hospital, Puducherry, India with the chief complaint of early loss of deciduous and permanent teeth and mobility in remaining teeth. The patient was referred to get dentist opinion by the department of pediatrics where he had been treated for the enteric fever. The past dental history revealed that the deciduous teeth had erupted normally but had exfoliated gradually by the age of 3-4 years. All permanent teeth had a normal eruption pattern, but later the teeth had shown mobility and subsequent loss of all incisors. Medical history revealed that the patient had been suffering from recurrent skin infections in his hands and feet since childhood with thickening and subsequent peeling of the skin. The family history showed a consanguineous marriage of the parents. The family members were not affected. The mother had a normal pregnancy and delivery. General examination revealed that the patient was thin built, anemic and showed the presence of marked hyperkeratosis of the skin of the hands and feet (Figures 2 and 3). The keratinized skin was clearly demarcated from the adjacent normal skin. Deep fissures were noted on the soles of feet (Figure 4). His nails and hair were normal. Patient had a reduced facial height and facial prominence due to resorption of the alveolar ridge and absence of teeth. Intraoral examination revealed edentulous area in anterior maxillary and mandibular ridge with normal mucosa and 11,12,14,21,22,31,32,41,42 were also missing. The gingiva was bright red in color, soft and edematous. On assessment grade 3 mobility was present in relation to

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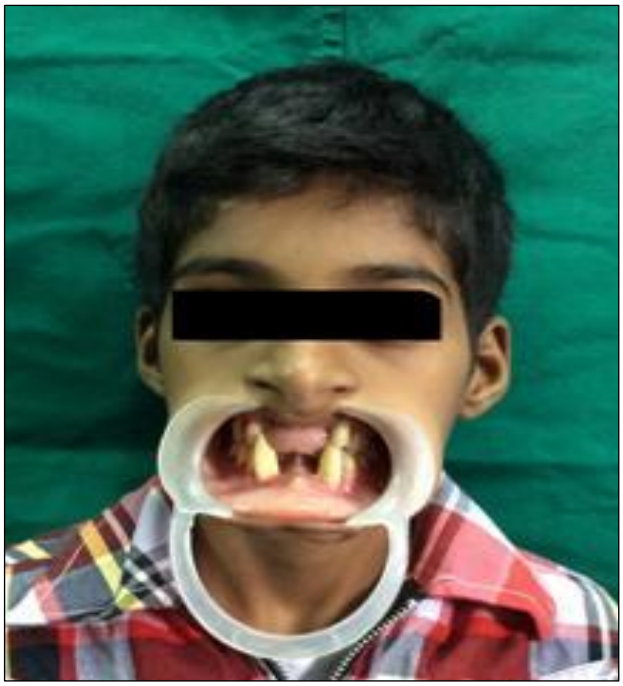

Figure 1: Facial profile

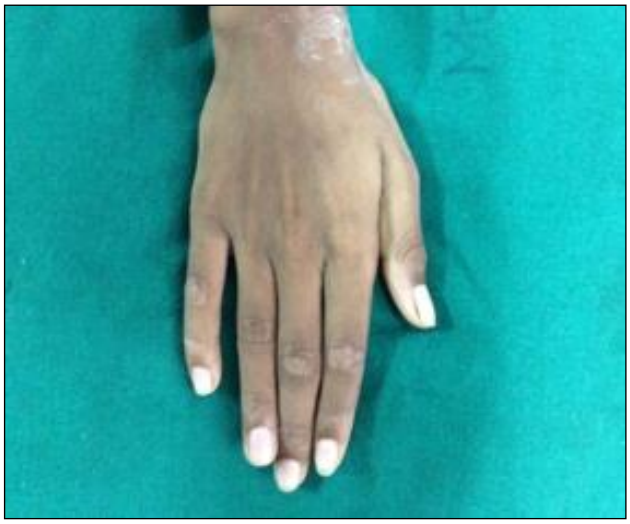

Figure 2: Hyperkeratotic patch on fingers

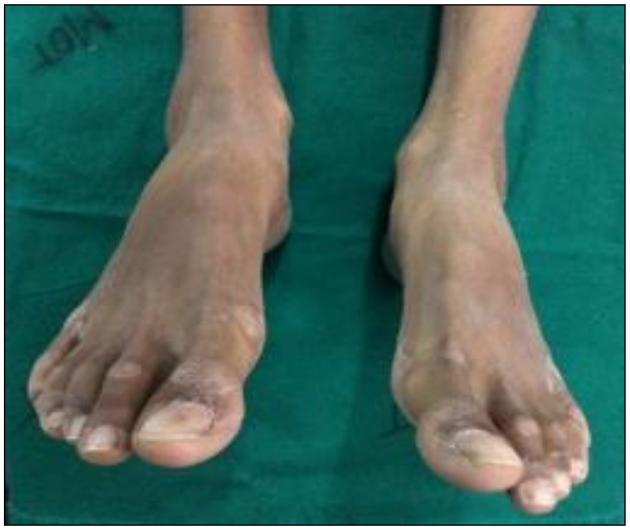

Figure 3: Hyperkeratotic patch on feet

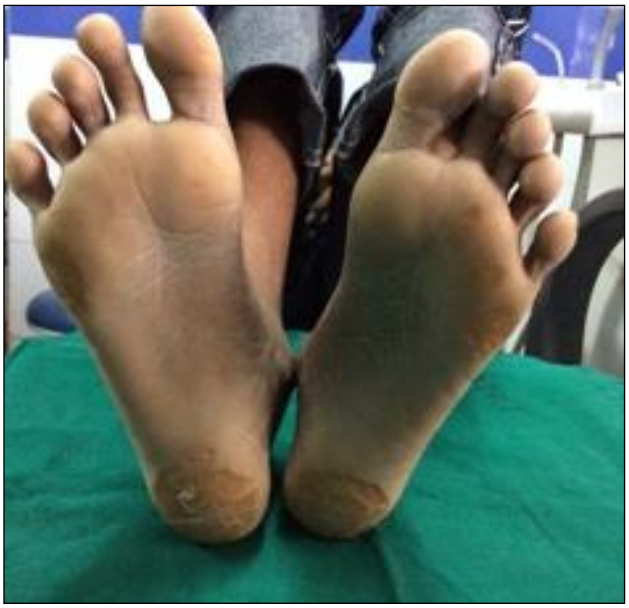

Figure 4: Plantar keratosis

15,25,33,43 grade 2 mobility in relation with 26, 36, 46 and remaining teeth were grade l mobility. Radiographic examination by Orthopantomogram and intraoral periapical radiographs showed extensive alveolar bone loss giving the teeth a characteristic "Floating in air" appearance (figure 5). Supernumerary tooth buds were also noted in relation to 14, 24, and 34 region. Hematological investigations, such as a complete blood count, blood chemistry profile, renal profile, liver profile tests produced results within normal results except low hemoglobin percentage. Based on the patient's history and typical dental, dermatological findings, PLS was diagnosed, and consanguinity was proposed as a risk factor.

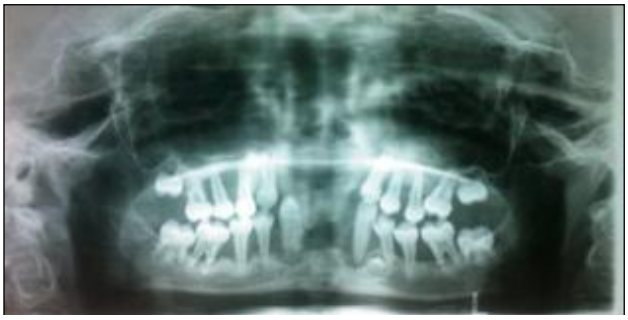

Figure 5: Orthopantamograph showing "floating in air appearance

DISCUSSION

Consanguineous marriages have been followed since the early existence of modern human beings. In populations of Middle East, North Africa, and south India consanguineous marriages are culturally and socially favored. In Arab communities, consanguineous marriage constitutes 20-50% of all marriages.[7, 9] It is believed that consanguineous marriages would preserve family dynamics and structure and provide cultural, social and economic benefits. Consanguineous marriages were highly significant in autosomal recessive diseases and increased the chance that both husband and wife will

carry any recessive gene that is being transmitted in the homozygous state in their children.

PLS is genetically inherited and appears to follow an autosomal recessive pattern, both parents were phenotypically healthy and carried the recessive gene for the syndrome to appear in their children. An increased prevalence of parental consanguinity around 20-40% has been reported in PLS patients.[7] PLS has a prevalence of 1-4 cases per million persons without any sex and racial predominance. Till date More than 300 cases of PLS have been reported in English literature worldwide.PLS is characterized by hyperkeratosis of the palms and soles combined with precocious periodontal destruction and shedding of the deciduous and permanent dentitions. Additional findings associated with PLS cases may include Dural calcification, pyogenic infections, nail dystrophy and hyperhidrosis.[4,9]

The etiopathogenesis of the PLS is not clearly understood and genetic, immunologic, or possible microbial etiologies have been proposed. PLS may be genetically determined and shown mutations affecting both alleles of the Cathepsin-C (CTSC) gene, located on chromosome 11q14.1-q14.3. The CTSC gene is expressed mainly in the epithelial regions such as palms, soles, knees and keratinized oral mucosa. These are generally the areas that are most commonly affected by PLS.CTSC gene is also expressed at high levels in various immune cells including polymorphonuclear leucocytes, macrophages, and their precursor cells. Mutations of CTSC gene in epithelial regions can lead to skin abnormalities results in hyperkeratosis on the palm and soles. CTSC gene mutation results in altered immune response to infection, which may affect the junctional epithelium integrity resulting periodontitis and tooth loss. Another important etiologic factor is immune mediated. CTSC gene is involved in a wide variety of immune and inflammatory responses. An alteration of the host defense due to decreased function of lymphocytes, polymorphonuclear leucocytes, helper/suppressor T cells ratio and monocytic function were also impaired in PLS.[10] Therefore, mutation of CTSC will result in loss of immunological responses and interference in phagocytic activity leading to severe periodontal tissue destruction in PLS. Microbiologically, the subgingival plaque found in the periodontal pockets of PLS patients resembles a typical periodontitis- associated microflora and has shown a predominance of gram-negative anaerobes. The presence of virulent gram - negative anaerobic pathogens Actinobacillus Actinomycetemcomitans, Porphyromonal gingivalis, Fusobacterium nucleatum and Treponema denticola organisms have been demonstrated in several studies.[4,10-12] Recent studies have demonstrated a greater prevalence of Actinobacillus Actinomycetemcomitans in patients with PLS and its significance in the pathogenesis and progression of aggressive periodontitis. The complex etiopathogenesis of PLS shows that successful treatment of the periodontal problem of this syndrome remains challenging.

Clinically, skin lesions of PLS most commonly manifest between 6 months to 4 years of age, coinciding with the eruption of primary teeth.[4] Skin lesions appear as white, light yellow, brown or red plaques which undergo crustation, cracking and deep fissuring. The well demarcated erythematous keratotic scaly plaques may occur focally, but usually involve the entire surface of the palms and soles and may extends to dorsal surface, often there is associated hyperhidrosis of the palms and soles resulting in a foul smelling odor.[13] Nail changes such as transverse grooving and fissuring are apparent in advanced cases. Oral manifestations of PLS appears almost simultaneously with the onset of skin lesions. Primary teeth are erupted at the expected age and in normal sequence, but their eruption is associated with severe gingivitis in the absence of any local etiological factor. Gingiva appeared erythematous, edematous and bleeds readily on probing. The periodontal pockets rapidly deepen with severe alveolar bone loss. Typical dental features of PLS are hypermobility, drifting, migration and exfoliation of teeth. At the age of 4-5 years, the primary teeth are exfoliated, and the child becomes completely edentulous with normal appearing gingiva.[14] After the eruption of permanent teeth, the same cycle continues and by the age of 13-15 years all of the permanent teeth are lost. Radiographic examination of PLS patients are characterized by the severe alveolar bone loss resulting “floating in air” appearance of teeth.[11,4] In addition to the dental and dermatologic findings, PLS patients may have impaired neutrophil, lymphocyte or monocytes function and an increased susceptibility to microbial infection, leading to recurrent pyogenic infection of the skin. A Pyogenic liver abscess is also recognized as a complication of PLS because of impairment of the immune system.

The management of PLS is challenging and requires a multidisciplinary approach with the active participation of the dental surgeon, dermatologist, and pediatrician. A definite treatment regime has not been reported; however, to control periodontal destruction, several treatment modalities have been suggested including conventional periodontal therapy, oral hygiene instructions, and systemic antibiotics. Early extraction of primary teeth has also been advocated to eliminate periodontal pathogen; so that the patient’s permanent teeth can erupt in a safer environment. Successful treatment of PLS periodontitis using both Amoxicillin and metronidazole (250mg /tid for 10 days or 6 weeks) followed by supportive periodontal therapy every 3 to 4 months was reported.[9] The periodontitis in PLS is usually difficult to control due to poor prognosis, and the course of the disease is highly unpredictable. Prosthodontic management of PLS patient is an age specific specialty treatment involving initial replacement with partial dentures or complete denture and future consideration for implant supported prosthetic dentures. Pre prosthetic surgical techniques have been introduced for better retention and stability of dentures. Modern dental implants are also considered for PLS

patients who provide better stability and retention of prosthesis and improve esthetics and masticatory efficiency.[15] Skin lesion of PLS patient are usually treated with anti-inflammatory emollients. The use of Oral retinoids such as acitretin, etretinate and isotretinoin were reported to be beneficial in both dermal and dental lesions of PLS.[12,16] However, isotretinoin should be used carefully because of its teratogenic effects. It is reported that etretinate and acitretin modulate the course of periodontitis and preserve the teeth if started during the eruption of permanent teeth it may end up with normal dental-development.

CONCLUSION

Consanguineous marriages are often associated with a risk of congenital malformations and autosomal recessive disease.PLS is an autosomal recessive trait. The etiopathogenesis of the syndrome is not clearly understood and genetic, immunologic, or possible microbial etiologies have been proposed. Higher prevalence of PLS has been reported when parental consanguinity is involved. Rather than discouraging consanguineous marriages in population with long held such tradition, guideline for screening consanguineous couples are needed and ensuring access to premarital and preconception counseling service is the logical way to manage genetic disease such as PLS.

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