CASE REPORT

Papillon-Lefèvre Syndrome: Detrimental Periodontal Condition in the Affected Individuals

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ABSTRACT

This paper aims to highlight the detrimental periodontal condition in patients with Papillon-Lefèvre syndrome (PLS) and the pivotal role of a Periodontist in the diagnosis of the condition. PLS is also known as palmo-plantar keratosis (PPK) with an unusual periodontal status. Uncontrolled early-onset periodontitis, which affects both primary and permanent dentitions alike, is a hallmark of the syndrome. PLS patients exhibit defected neutrophil chemotactic function due to substandard activity of Cathepsin C (CTSC) gene. The result is the failure of elimination of periodontal pathogens that leads to severe periodontal destruction. We report a case of an 11 years old Pakistani girl affected with PLS whose parents are consanguineously married. Since PLS is a rare autosomal recessive disorder and multiple consanguinity in a family, increases the risk of the occurrence of the syndrome in the off springs, the case report also highlights the importance of pre-marital genetic mapping and conception counseling for the families.

Keywords: Papillon-Lefevre Disease; Cathepsin C; Periodontitis; Palmoplantar keratosis.

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INTRODUCTION

Papillon-Lefèvre syndrome (PLS), a condition illustrated by palmo-plantar keratosis (PPK) and severe early onset periodontitis, was described in 1924 by two French practitioners Papillon and Lefévre[1] Associated features include intra-cranial calcifications and susceptibility to bacterial infections[2]. PLS is prevalent in about 1-4 cases in a million. Haneke[3] concluded that PLS has no gender or racial predominance and consanguinity is a major risk factor in all of the reported cases. As early onset aggressive periodontitis affecting both the primary and permanent dentition is the striking feature of this syndrome, periodontal health in the affected individuals warrants attention.

CASE REPORT

An 11-year-old girl came to the division of Periodontology, Ziauddin College of Dentistry, Karachi with the chief complain of early exfoliation of teeth along with hyper mobile remaining teeth. These conditions were first noticed around the age of 4 when the patient had deciduous dentition. Patient presented with the medical history of cutaneous keratotic plaques on her palms, soles, elbows and knees (Figure 1, 2) for which she was already being treated by the dermatologist. The skin lesions were first noticed when the patient was 2 years old and the lesions become more severe during cold weather. The skin was rough and dry presenting well-circumscribed, scaly plaques yet the hair and nails appeared clinically normal.

Figure 1: Palms demonstrating scaly keratotic plaques.

Figure 2: Soles of the patient demonstrating scaly dry skin.

The pattern of severe mobility for 5-6 months after complete eruption and subsequent exfoliation was observed for both primary and permanent dentition. The patient is otherwise healthy, school going girl possessing good comprehension skills. Family history advocates that her younger brother, who is 9 years old, is also displaying similar oral and cutaneous manifestations. The parents of the girl are healthy, present no signs of the syndrome, come from a low socio-economic background and have a consanguineous marriage.

On intra oral examination, the patient presented with hyperemic edematous gingiva with multiple periodontal abscesses, gingival bleeding, hypermobile teeth and multiple missing teeth (Figure 3). The gingiva around the present permanent teeth was erythematous, soggy and swollen along with deep periodontal probing depth, which bled on probing (Figure 3). Due to associated pain, the patient had stopped brushing her teeth, which led to aggravated symptoms. An (orthopantomagram) OPG X-ray was advised. On examination, it was observed that there was severe generalized bone resorption and the teeth presented with the classic "floating in the air" appearance (Figure 4). Majority of the remaining teeth in the mouth presented with some degree of mobility along with hypermobility of a few teeth. The patient was advised routine clinical investigations including complete blood picture (CP), liver function transaminase (LFT), total bilirubin, alkaline phosphatase and C-reactive protein (CRP). All of the lab findings were normal except CRP, which was raised.

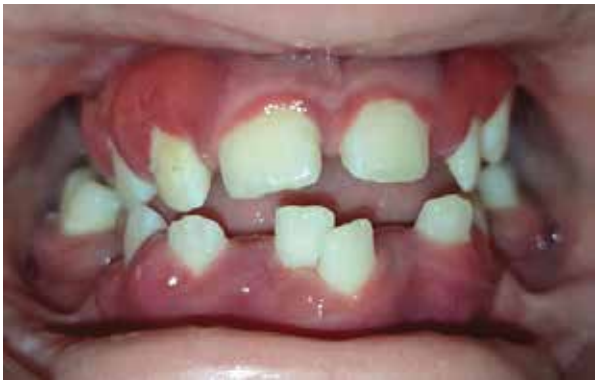

Figure 3: Intra oral picture showing severe gingivitis, missing teeth and hypermobile permanent teeth.

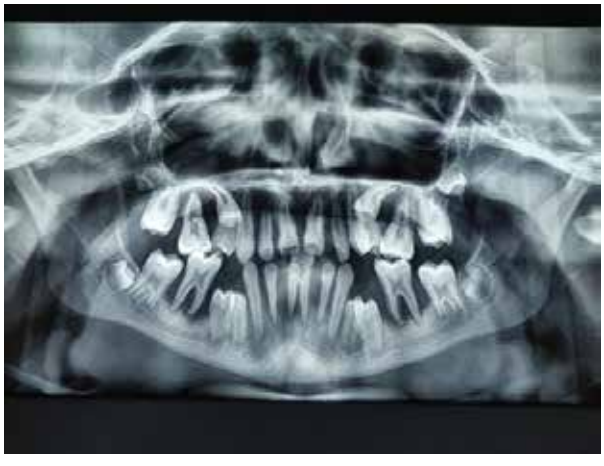

Figure 4: OPG demonstrating generalized severe bone loss and floating in the air - appearance for permanent teeth.

Based on the medical and dental findings, the diagnosis of PLS was established. Patient was counseled and thoroughly explained about the syndrome and the treatment options. A written consent form was explained to the minor and her mother and was signed by the parents before starting the treatment protocol. Scaling and polishing were administered with 0.2% chlorhexidine gluconate irrigation in deep pockets. Antibiotic coverage (Amoxicillin 250mg t.d.s and metronidazole 200mg t.d.s) for 7 days was prescribed. Mouth rinse with 0.12% CHX (b.i.d for 14 days) was prescribed as well. The patient was

scheduled for supportive periodontal therapy every 2 months, which included chemical and mechanical periodontal debridement protocol (Figure 5). Due to the poor prognosis of the "floating teeth", it was planned to extract the teeth and prosthetic rehabilitation was suggested. It was planned to provide a set of partial dentures to the patient with a possibility of dental implants in future. Following the extraction of patient's mandibular anterior teeth, an interim partial denture was fabricated for her lower arch to restore her function and aesthetics.

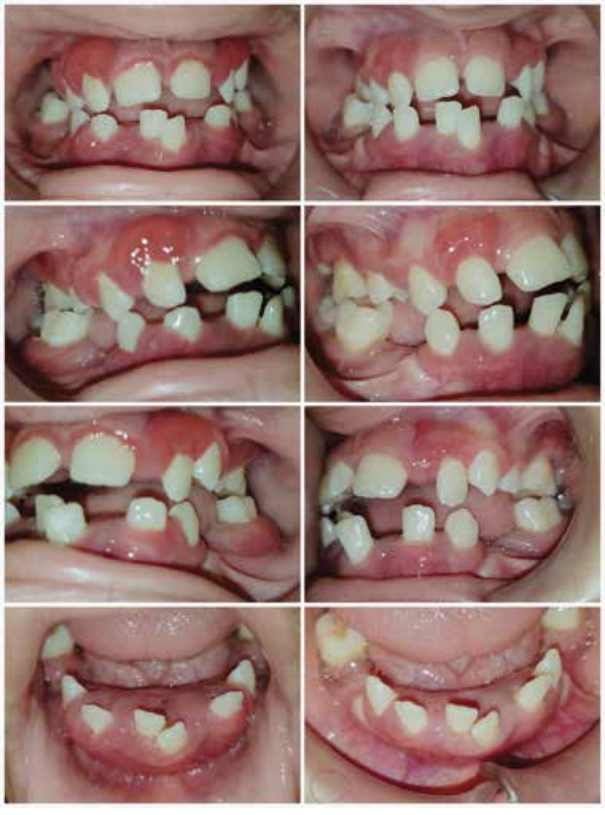

Figure 5: Periodontal health improvement after administration of non-surgical periodontal treatment - 4 weeks follow up.

DISCUSSION

Papillon-Lefèvre syndrome (PLS) is a genetically inherited autosomal recessive disorder whereby the clinically healthy parents, with no family history of the disorder, possess the autosomal gene for the syndrome, which manifests in their progenies[4]. When two carrier parents mate, there arises a 25% chance that the resulting child would be affected with the syndrome, regardless of the gender[5,6]. In the communities where the consanguineous marriages are practiced frequently, there is a chance that the gene for this disorder is endemic in the community, increasing the probability of both the parents to possess the gene, which would lead to increased risk of the occurrence of disorder in the offspring [5].

In communities where parental consanguinity is uncommon, there is a 2-3% risk of a congenital disorder, which accounts for mere 0.17% risk of developing an autosomal recessive disorder. Whereas when compared to some groups of Middle East or Pakistani origin, cousin marriages associated disorders almost double in the number for the prevalence of congenital disorders. A fairly recent prospective cohort study by Wright et al[7] included 13,776 babies, recruited between the period of 2007 and 2011, presented that 37% of the babies of Pakistani origin were the result of consanguineous marriages. The study also reported an alarming doubling of the risk for congenital anomaly, which was associated with consanguinity and of the affected, 6% of the progenies, had first-cousin marriage parents where as 5% of the affected babies had distant but related parents[8].

A higher incidence of PLS has been reported among inter-cousin marriages communities and racial populations than the previously reported studies[7]. The current case follows the typical reported pattern where the parents are Pakistani, consanguineous and phenotypically healthy, having two (one boy one girl) out of three children affected with PLS. Consanguinity is a common practice in their family. The associated deteriorating oral and cutaneous symptoms in children with PLS affect the functional, aesthetic, psychological and social well-being of these growing children.

Severe early onset periodontitis is a hallmark of the PLS syndrome. It becomes clinically apparent at the age of 2-3 years[9]. Primary and secondary teeth erupt in the usual sequence with the normal timing, structure and anatomy. However, it has been associated with the severe gingival inflammation, redness, swelling, bleeding, associated fetid odor and difficulty in eating due to hypermobility of the teeth. There is a consequent premature exfoliation of all the deciduous teeth well before their successors erupt by the age of 4-5 years. Some studies suggest that the erupting teeth may exhibit incomplete root formation or the dentition might present as microdontia. Permanent dentition follows the same sequence of events. Without intervention, the patient will lose majority of their permanent teeth by the age of 16 years. Consequently, affecting the patient's routine functional as well as social life.

Periodontitis in these individuals is a result of failure to remove periodontal pathogens. Aggregatibacter actinomycetemcomitans is the principal pathogen responsible for progression of periodontal infections[10]. These patients exhibit defective immune response because of lack of Cathepsin C (CTSC) gene functioning that leads to deficiency in neutrophil serine protease. This deficiency consequently results in decreased chemotactic activity of the neutrophils and failure of the neutrophils to produce extracellular traps. The serine proteinases

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also play a vital role in immunologic response including activation of phagocytes, signaling them to destroy the bacteria while simultaneously activating T-lymphocytes. Therefore, deficiency of Cathepsin-C enzyme results in exaggerated liability to infection and destruction of tissues. These dysregulations in the function of immune cells explain the excessive tissue destruction and severe periodontitis in PLS[11].

CTSC gene is expressed in epithelial cells, the areas commonly affected in the PLS syndrome, for instance, keratinized oral gingiva, palms, soles and the knees. The defective expression of CTSC exhibits its affects on all these areas in the affected patients. CTSC is also expressed in immune cells including poly morphonuclear neutrophils (PMNs), macrophages and the immune precursor cells[4]. The hyperactive neutrophil in the patients with PLS releases higher level of proinflammatory cytokines and exhibits reduced antimicrobial defense while simultaneously adding to the oxidative stress. Despite the defective functional ability of the neutrophils, the systemic immunodeficiency is surprisingly less pronounced in PLS patients with just 20% of the affected individuals predisposed to the risk of recurring infections, yet the periodontal destruction is significantly aggressive. Therefore, a Periodontist will be able to detect the unusual pattern at an early age and help the patient seek treatment. In all the reported cases of PLS, the patient usually was already under treatment for the skin conditions whereas the unusual presentation of oral health had not been noticed early. The particular case reported in this article follows the same pattern.

It is also necessary to emphasize the importance of genetic counseling for such families to make them aware of the potential risk of affected off springs. Premarital screening and preconception counseling programs are required to raise general awareness regarding the increase in the risk of genetic diseases in consanguineous marriages. Such structured programs will definitely help in reducing the number of individuals who suffer from untreatable syndromes. The awareness will save the parents and the off spring from life distressing predicament. For the pre conception counseling in consanguine marriages, it is pivotal to distinguish between families who present a known genetic disorder and the families with no known genetic or inherited disorder. Careful and detailed family history along with the formulation of four-generation lineage including, offspring, siblings, parents, aunts and uncles, grandparents, nieces and nephews and first cousins is mandatory.

With approximately one billion of the population residing in the areas and communities, where consanguinity is deep rooted, there is an absolute shortage of premarital counseling. It is interesting to note that in the regions where cousin marriages are usual, there exist discrepancies even among the healthcare professionals in counseling for cousin marriages and their potential detrimental consequences. With consanguinity now an established factor for PLS[5], it is advocated that families with increased risk factors be identified and genetic counseling should be taken up whenever feasible.

CONCLUSION

Early diagnosis and timely intervention is important in the cases of PLS to avoid the threat of being left edentulous at a prime age if left unmanaged. A periodontist plays the most important role in diagnosing such cases at its earliest as the unusual pattern of severe periodontitis and premature exfoliation of teeth is the characteristic presentation of the syndrome. A multidisciplinary protocol is recommended for the comprehensive management of such cases. Inter cousin marriages resulting in increased number of such cases advocates a well-structured premarital genetic counseling program to educate the communities regarding potential risks of the consanguineous conception.

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CONFLICT OF INTEREST

There was no conflict of interest among the authors.

PATIENT CONSENT

The patient was explained the case thoroughly and the minor assent along with the consent from her mother was obtained to publish the case and pictorial information strictly for the academic purposes only. Patient's personal information will remain confidential.

AUTHOR'S CONTRIBUTION

AH and ZHC diagnosed the case. AH conceived the idea, wrote the manuscript, provided periodontal treatment to the patient and counseled the family for the proposed treatment. HRB helped in the prosthetic rehabilitation of the patient.

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