PapillonLefevre Syndrome: Report of a Case Successfully Treated with Acitretin

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ABSTRACT

Introduction: Papillon-Lefevre syndrome (PLS) is a rare syndrome of autosomal recessive inheritance characterized by palmoplantar hyperkeratosis and early onset of a severe destructive periodontitis, leading to premature loss of both primary and permanent dentitions. The etiopathogenesis includes a genetic basis for susceptibility to specific virulent pathogens but a recent report has suggested that the condition is linked to mutations of the cathepsin C gene. Effective treatment includes extraction of primary teeth, systemic Acitretin, and antibiotics along with topical keratolytics and professional teeth cleaning.

Case report: This paper presents our experience with acitretin therapy in a case of PLS, who had an excellent response in palmoplantar skin lesions within four weeks.

Conclusion: As dentists play a significant role in diagnosis and management of PLS, this case report is an effort to create awareness among the dental fraternity.

Keywords: Papillon-Lefevre syndrome, palmoplantar hyperkeratosis, Acitretin

INTRODUCTION

In 1924, Papillon and Lefevre described a brother and sister with a condition characterized by palmoplantar hyperkeratosis (keratoderma) associated with severe, early onset periodontitis and premature loss of primary and permanent teeth. Gorlin et al added calcification of the falx cerebri to the syndrome, converting it into a triad. Variable findings in the syndrome include retardation of somatic development, follicular hyperkeratosis, nail dystrophy, and hyperhidrosis.[1,2]

The prevalence of PLS is 1-4 per million individuals with no sex predilection and no racial predominance. A genetic predisposition, with greater frequency of occurrence in offsprings of parents with consanguinity, has been reported.[3] In addition to genetic alterations, several environmental and host factors are involved in the PLS periodontitis including (a) specific virulent bacterial and viral infection of periodontium, particularly Actinobacillus actinomycetemcomitans, cytomegalovirus, and Epstein-Barr type 1 virus; (b) impaired neutrophil chemotaxis, migration, and phagocytoxic functions, and increased superoxide production (c) reduced functional activity of monocytes elicited by decreased phagocytosis, increased tendency to aggregate, and impaired Fc-receptor function; (d) decreased mitogenic activity of lymphocytes, and reversed ratio of T-helper to T-killer cells (e) degenerative changes of plasma cells and elevation of serum immunoglobulin (IgG) and (f) disrupted functioning of fibroblast and cementoblast along with defective periodontal ligament attachment and gingival epithelium leading to imbalanced collageno-lytic activity in the periodontal ligament. Accumulated etiopathogenesis suggests that PLS is a complex interaction between immune-mediated deficiencies in the host defense mechanism and inherited genetic defects.[4,5] An increased susceptibility to infection has been reported in approximately 25% of Papillon-Lefevre patients.[1]

CASE REPORT

A fourteen year old girl reported to the outpatient department complaining of loose teeth and difficulty in chewing. [Fig.1] Patients also complained of peeling of the skin of the hands and feet. On further conversation, patient told that her parents were first cousins and had consanguineous marriage. Parents and other members of the family were not affected. On general examination, the patient had overall normal physical and mental development. Extra oral examination demonstrated keratoderma on the palmo plantar aspects of hands, feet, lateral aspect of the legs, knees and elbows. On intraoral examination the patient had permanent dentition with gingival inflammation, deep periodontal pockets along with mobility affecting all the teeth. [Fig.1] Orthopantomogram revealed generalized destruction of alveolar bone while lateral skull projections did not reveal any calcific areas within the skull. [Fig.1] Baseline investigations like complete blood count, liver function tests, electrolytes, fasting cholesterol and triglycerides were within normal limits.

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Thus the patient was diagnosed to be suffering from Papillon Lefevre Syndrome.Treatment consisted of oral Acitretin 10mg per day, Cotrimoxazole (200:40) and topical keratolytics which included 6% coal tar, sulphur and salicyclic acid (salytar). Initially the patient was put on Acitretin 10mg once daily for two days of every three for 8 weeks and then every alternate day for next 8 weeks and then once in three days for another 8 weeks. Within 4 weeks, marked regression of the palmoplantar keratoderma was seen. (Fig.2,3,4) Periodontal health also improved considerably. The patient was followed on the same maintenance dose for next six months and reviewed monthly. The baseline investigations were repeated every 6 months. At one year follow up visit we noticed almost healthy skin though there was history of exacerbations during the winters.

DISCUSSION

Papillon Lefèvre syndrome is called so because it was described by Papillon and Lefèvre in 1924. The hallmark of this syndrome is diffuse palmoplantar hyperkeratosis and juvenile periodontitis. Initial manifestations are noticed during first decade of life in the form of hyperkeratosis seen over soles and dorsal surface of the hands and feet. Erythematous hyperkeratotic plaques may also be present at the elbows, knees, and trunk. Severe periodontitis affecting both primary and permanent dentition in 3- 4year old young children is seen.[3]
In PLS, there is eruption of primary teeth in the normal sequence, with the teeth being of normal form and structure. No delay in eruption timings is seen. Severe gingival inflammation and generalized aggressive periodontitis leading to tooth mobility has been reported with erupting dentition. As a result of which primary teeth are exfoliate by the age 4 or 5 years. After exfoliation of the primary dentition the gingival inflammation resolves only to revert back in same sequence with eruption of permanent teeth. Thus, permanent dentition is lost by 15-17 years of age. Severe resorption of alveolar bone gives the teeth characteristic 'floating-in-air' appear-

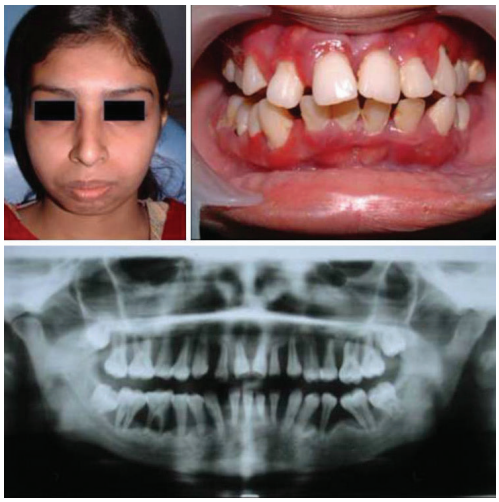

Figure-1: Extra Oral profile, Intraoral Photograph showing severe periodontitis and OPG showing generalized bone loss.

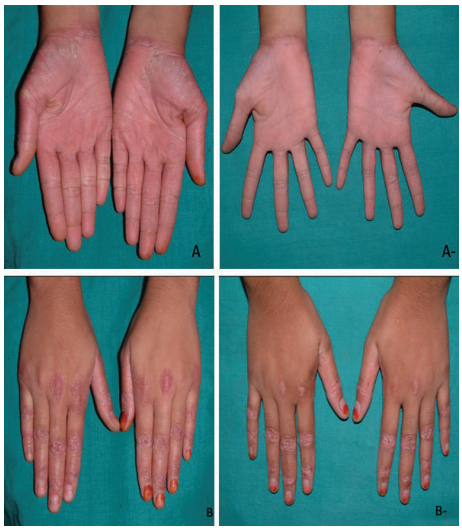

Figure-2: A, A: Pre and post treatment photograph of palmar aspect of both hands. B, B: Pre and post treatment photograph of both hands (front view)

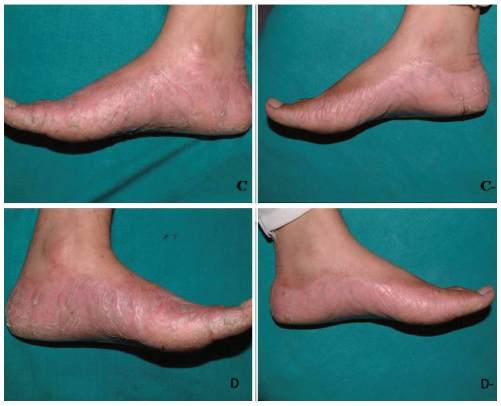

Figure-3: C, C: re and post treatment photograph of medial surface of right leg. D, D: Pre and post treatment photograph of medial surface of left leg.

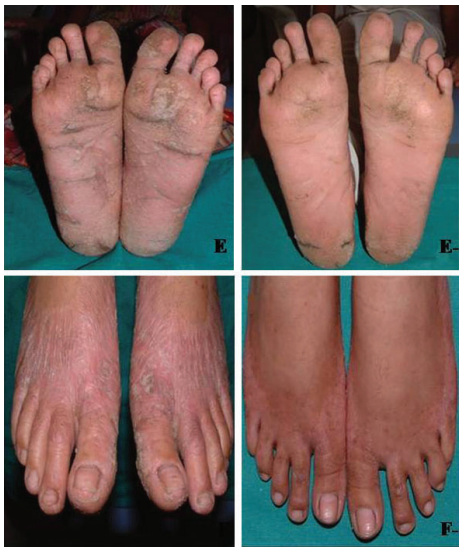

Figure-4: E, E: Pre and post treatment photograph of plantar aspect of both legs. F, F: Pre and post treatment photograph of both legs (front view)

ance on dental radiographs. Palmoplantar keratosis may be in the form of mild psoriasiform scaly skin to hyperkeratosis involving skin of entire hands, feet, elbows and knees.[2,6]
Especially in winter, palmoplantar hyperkeratosis worsens with painful fissures, similar to our case, thereby limiting routine activities and necessitating systemic treatment.[7] The etiology of PLS is debatable, but most widely accepted hypothesis states it to be due to mutations in one or both the alleles of cathepsin c gene which results in loss of function. Cathepsin c gene, located on chromosome 11q14.1-q14.3 is expressed in palms, soles, knees, and keratinized oral gingiva. All these regions are commonly affected by PLS It is also expressed at high levels in various immune cells including polymorphonuclear leukocytes, macrophages, and their precursors. It encodes a cysteine-lysosomal protease also known as *dipeptidyl-peptidase I* which functions to remove dipeptides from the amino terminus of the protein substrate. It also has endopeptidase activity. Mutations in cathepsin c gene result in PLS syndrome, haim-munk syndrome, and prepubertal periodontitis.Severe early-onset periodontitis in all of these three conditions.[8,9]
Haim munk syndrome is the most closely mimicking entity which is defined by tapered, pointed phalangeal ends, claw like volar curves, pes planus and arachnodactyly.[6,10,11] But none of these were seen in our case. Conditions like acrodynia, hypophosphatasia, histiocytosis X, leukemia, cyclic neutropenia, Takahara's syndrome are associated with periodontitis and premature loss of teeth but no palmoplantar hyperkeratosis. Other group of closely resembling conditions Unna Thost, mal de Meleda, Howel-Evans syndrome, keratosis punctata, keratoderma hereditarium mutilans (Vohwinkel's syndrome), and Greither's syndrome but these entities are not associated with periodontopathy.[1] Histopathological findings of affected skin have not been well described in the literature. Reported histopathological findings include hyperkeratosis or parakeratosis, acanthosis, and slight perivascular inflammatory infiltrate.[5,11] A multidisciplinary approach is essential for the effective management of patients with PLS. Keratolytics are the drug of choice for skin manifestations in PLS. Salicylic acid, coal tar and sulphur may be added to the regimen as adjuncts. Oral retinoids including acitretin, etretinate, and isotretinoin are helpful to treat both the keratoderma and periodontitis associated with PLS.[12] For obvious reasons, the outcome of treatment is better if initiated during the eruption and maintained during the development of the permanent teeth. Effective periodontal management includes antibiotics, thorough oral prophylaxis and extraction of the primary teeth. Role of etretinate and acitretin lies in preserving the teeth by modulating the course of periodontitis. Antibiotics are prescribed to control the active periodontitis so as to prevent spread of bacteria in blood which might cause pyogenic liver abscess.[5,13]

CONCLUSION

To conclude, we have tried to create awareness among medical fraternity about a not-so-common disease which has a negative psychological impact of lives of young children. Early dental evaluation and parental counselling as a part of preventive treatment is essential for providing complete psychosocial rehabilitation for PLS patients.

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