Case Report

Papillon lefevre – A rare syndrome

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Abstract

Papillon lefevre syndrome (PLS) belongs to a heterogeneous group of skin diseases that are characterized by hyperkeratosis of palms and soles and presence of severe and early onset periodontitis. Genetic studies have shown that mutation in the major gene locus of chromosome 11q14 with the loss of function of cathepsin C (CTSC) gene is responsible for PLS. Loss of CTSC function is responsible for the severe periodontal destruction seen clinically. This report represents classical signs and symptoms of PLS in a 6 year old girl.

Key words

Aggressive periodontitis, Cathepsin C gene, Papillon lefevre syndrome.

Introduction

Papillon-Lefèvre syndrome (PLS) is characterized by erythematous palmoplantar hyperkeratosis and severe periodontal disease. Dermatological as well as oral signs vary considerably between affected subjects [1]. The condition is inherited as an autosomal recessive trait [2] and linked to mutations of the cathepsin C gene [3, 4]. Cathepsin C is a lysosomal cysteine protease that activates several granule serine proteases expressed in bone marrow derived effector cells of myeloid and lymphoid series [5]. These proteases are implicated in a variety of immune and inflammatory processes, including cell-mediated cytotoxicity, phagocytic destruction of bacteria, local activation and deactivation of cytokines and other inflammatory mediators, and extracellular matrix degeneration [6]. Cathepsin C is normally expressed in palmar, plantar, and gingival epithelium [7], but its involvement in epithelial desquamation or its significance in gingival epithelium is unknown [8]. While several cathepsin C gene mutations have been identified [9], the correlation to the disease's phenotypic expression is still obscure. The aggressive periodontal inflammation leads to premature loss of primary and permanent teeth. Clinical observations and investigations have led to various theories regarding possible etiologic

mechanisms, including altered immune response [10-13], underlying tissue pathology [14, 15], and virulent and aggressive periodontal flora. *Actinobacillus actinomycetemcomitans* is a periopathogen of key importance in periodontal infections and has often been identified in periodontal lesions in PLS patients [15-19]. Others, however, have found flora without any particular periodontal pathogens [20, 21].

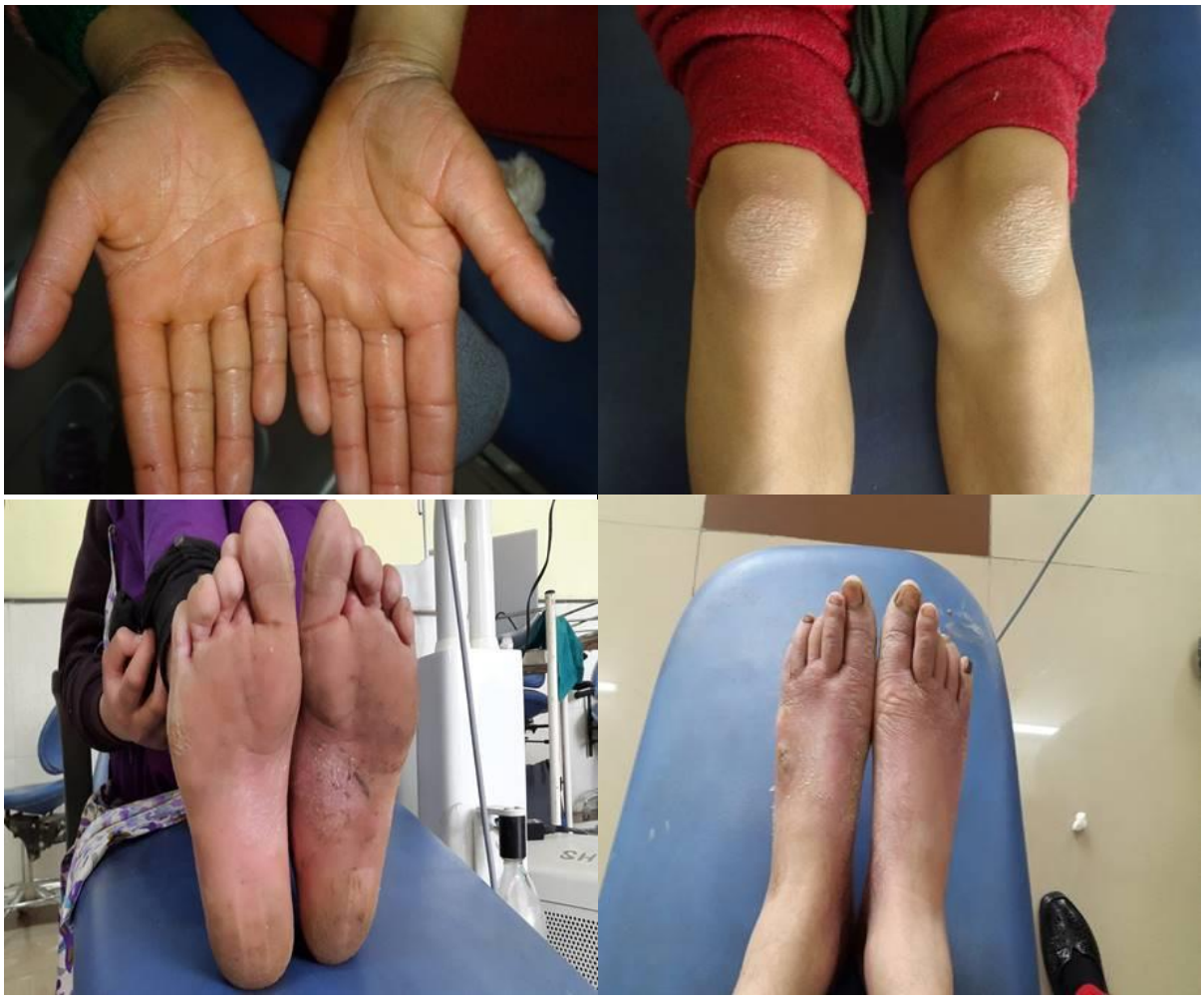
Case report

A 6 year old girl was presented to Department of Periodontics, Govt. Dental College and Hospital, Srinagar. Her father noticed mobility in relation with some of her permanent teeth. The patient was referred to our Department for general dental care by the Department of Dermatology where she had been diagnosed with PLS. She was the first child born to apparently healthy non consanguineous parents. Typical clinical signs of the disease were seen during the child's 1st year of life. However, he had not sought any treatment until now.

General and extra-oral examination

The family history revealed consanguineous marriage of the parents. The parents and other family members were not affected. Patients had overall normal physical and mental development. Extra-oral examination of revealed yellowish, keratotic, confluent plaques affecting the skin of her palms and soles. Well circumscribed, psoriasiform, erythematous, scaly plaques were also present on the elbows and knees bilaterally along with dystrophy and transverse grooving of the nails (**Figure – 1**).

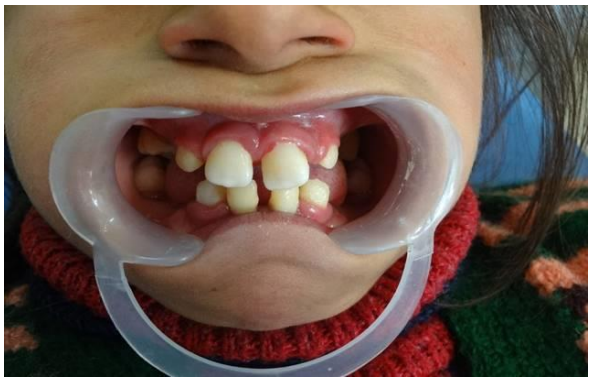
Figure - 1: Patient presenting with yellowish, keratotic, confluent plaques affecting the skin of palmar surfaces of hands, knees, keratotic plaques on soles, dorsal surfaces of feet.



Intraoral examination

On intraoral examination revealed severe gingival inflammation, abscess formation, and deep periodontal pockets were noticed. Severe mobility affecting all the permanent teeth, with heavy deposits of plaque and calculus and halitosis were also present (**Figure – 2**). All primary teeth were exfoliated.

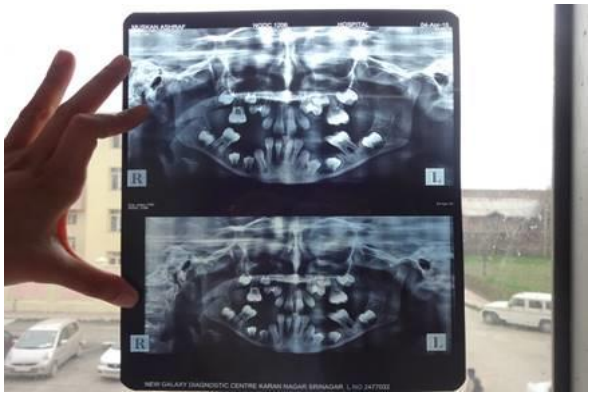
Figure - 2: Intraoral anterior view.



Radiographic findings

Orthopantogram showed extensive alveolar bone loss in all remaining teeth. The alveolar bone around the mobile teeth was devoid of definable lamina dura. An extensive alveolar bone loss was noted, a "floating in air appearance," which were extracted afterwards (**Figure – 3**).

Figure - 3: OPG showing severe generalized destruction of alveolar bone support.



Laboratory investigation

Laboratory investigation was carried out, which included hematological and biochemical assessment. The results were within normal limits.

Treatment

A multidisciplinary approach involving the Dermatologist, Periodontist, Pedodontist and Pediatrician is important for the overall care of patient with PLS.

Periodontal treatment

Aim of periodontal treatment is to eliminate the reservoir of causative organisms. It is generally agreed that the response to local debridement or to systemic antibiotic alone or in combination provide at best a transitory response [22-24].

Treatment given

- Conventional periodontal treatment in the form of scaling and root planning
- 0.2% chlorhexidine gluconate mouthwash and oral hygiene instruction was employed to control disease activity
- Systemic antibiotic treatment was given for 4 weeks amoxicillin (20-50 mg/kg/d) + metronidazole (15-35 mg/kg/d) in divided doses every 8 h as an adjunctive with conventional treatment
- Teeth with hopeless prognosis were extracted
- In teeth having deep periodontal pockets, periodontal flap surgery was done
- To restore masticatory function, partial dentures were inserted
- Maintenance visits of 2- 3 months were planned.

In recent years, dental implant offers not only considerable better stability and retention of prosthesis, but also improved comfort, masticatory efficiency and esthetics. There is data available that dental implants are successful mode of rehabilitation in patients with PLS [25]. We have planned for implant supported prosthesis in patients after growth period is over.

Dermatological treatment

The skin manifestations of PLS are usually treated with emollients. Salicylic acid and urea may be added to enhance their effect. Oral retinoids including acitretin, etretinate and

isotretinoin are the mainstay of the treatment of both the keratoderma and periodontitis associated with PLS [26]. After 8 weeks of oral acitretin, there was a dramatic improvement with marked reduction of keratodermas. Treatment may be more beneficial if it is started during the eruption and maintained during the development of the permanent teeth.

Discussion

PLS can adversely affect growing children psychologically, socially, and aesthetically. Typically the parents are not affected and there is no family history of the disease. Higher prevalence has been reported when parental consanguinity is involved, but no predilection for gender or race has been documented [27, 28]. Phenotypically, the parents were healthy and there was no family history of the disease, suggesting an autosomal recessive pattern of inheritance. In case of PLS, the inflammatory infiltrate at the sites of periodontal infection is not under regulatory control.

Increase neutrophil influx and retention of inflammatory infiltrate and their proteases play a significant role in continued periodontal destruction. It makes difficult to control and limit periodontitis once lesions are established and disease becomes unresponsive to traditional periodontal treatment.

The clinical manifestations observed in our patient were hyperkeratosis of the palms, soles, elbows, and knees and generalized aggressive periodontitis, which resulted in loss of the primary and permanent teeth. Because the etiology and pathogenesis of PLS periodontitis is directly related to high levels of Actinobacillus actinomycetemcomitans, the use of an antibiotic that acts specifically on this pathogen has been claimed to be important for a successful treatment [28].

Prosthetic replacement in such patients is an age specific speciality treatment involving initial replacement with complete or partial dentures and future consideration for an implant supported prosthesis. It would provide immediate satisfaction to the patient in terms of esthetics and function. In the present case, prosthetic rehabilitation was considered in order to provide immediate satisfaction to the patient in terms of esthetics and function.

Conclusion

PLS is a rare autosomal recessive disorder. The conflicting findings of PLS management could be related to the severity of the condition, the age at which treatment was instituted, timing and duration of antibiotic therapy, professional supervision, supportive treatment plan and home care.

The complex etiopathogenesis of PLS means that successful treatment of the periodontal component of this syndrome remains challenging. It is hoped that with identification of the gene defect, better treatment modalities can be developed. In cases where patient reports late or not responding to periodontal treatment, dental implants are successfully advised.PLS threatens children and their parents with the prospect of edentulism if left untreated. Hence, early diagnosis and intervention is essential. Osseointegrated implants are an option for the future and can have a great impact psychosocially by restoring esthetics as well as function.

References

1. Hart T, Shapira L. Papillon-Lefèvre syndrome. Periodontol., 2000; 6: 88-100.
2. Gorlin RJ, Sedano H, Anderson VE. The syndrome of palmarplantar hyperkeratosis and premature periodontal destruction of the teeth. J Pediatr., 1964; 65: 895-908.
3. Toomes C, James J, Wood AJ, et al. Loss-of-function mutations in the cathepsin C gene result in periodontal disease and palmoplantar keratosis. Nat Genet., 1999; 23: 421-424.

4. Hart TC, Hart PS, Bowden DW, et al. Mutations of the cathepsin C gene are responsible for Papillon-Lefèvre syndrome. J Med Genet., 1999; 36: 881-887.
5. Pham CT, Ley TJ. Dipeptidyl peptidase I is required for the processing and activation of granzymes A and B in vivo. Proc Natl Acad Sci USA, 1999; 96: 8627-8632.
6. Hewitt C, McGormick D, Linden G, et al. The role of cathepsin C in Papillon-Lefèvre syndrome, prepubertal periodontitis, and aggressive periododontitis. Hum Mutat., 2004; 23: 222-228.
7. Rao NV, Rao GV, Hoidal JR. Human peptidyl-peptidase I. Gene characterization, localization, and expression. J Biol Chem., 1997; 272: 10260-10265.
8. Kimayai-Asadi A, Kotcher LB, Jih MH. The molecular basis of hereditary palmoplantar keratodermas. J Am Acad Dermatol., 2002; 47: 327-343.
9. Selvaraju V, Markandaya M, et al. Mutation analysis of the cathepsin C gene in Indian families with Papillon-Lefèvre syndrome. BMC Med Genet., 2003; 4: 5.
10. Celenligil H, Kansu E, Ruacan S, Eratalay K. Papillon- Lefèvre syndrome: Characterization of peripheral blood and gingival lymphocytes with monoclonal antibodies. J Clin Periodontol., 1992; 19: 392-397.
11. Ghaffer KA, Zahran FM, Fahmy HM, Brown RS. Papillon-Lefèvre syndrome: Neutrophil function in 15 cases from 4 families in Egypt. Oral Surg Oral Med Oral Pathol Oral Radiol Endod., 1999; 88: 320-325.
12. Liu R, Cao C, Meng H, Tang Z. Leukocyte functions in 2 cases of Papillon-Lefèvre syndrome. Clin Periodontol., 2000; 27: 69-73.
13. Firatli E, Gurel N, Efeoglu A. Papillon-Lefèvre syndrome. Analysis of peripheral blood lymphocyte subsets. J Clin Periodontol., 1996; 23: 823-825.
14. Lyberg T. Immunological and metabolic studies in two siblings with Papillon-Lefèvre syndrome. J Periodontol Res., 1982; 17: 563-568.
15. Preus HR. Treatment of rapidly destructive periodontitis in Papillon-Lefèvre syndrome. Laboratory andclinical observations. J Clin Periodontol., 1988; 15: 639-643.
16. Kleinfelder JW, Topoll HH, Preus HR, Muller RF,Lange DE, Böcker W. Microbiological and immunohistological findings in a patient with Papillon-Lefèvre syndrome. J Clin Periodontol., 1996; 23: 1032-1038.
17. Wiebe CB, Hakkinen L, Putnins EE, Walsh P, Larjava HS. Successful periodontal maintenance of a case with Papillon-Lefèvre syndrome: 12-year follow-up and review of the literature. J Periodontol., 2001; 72: 824-830.
18. Pacheco JJ, Coelho C, Salazar F, Contreras A, Slots J, Velazco CH. Treatment of Papillon-Lefèvre syndrome periodontitis. J Clin Periodontol., 2002; 29: 370-374.
19. Wara-aswapati N, Lertsirivorakul J, Nagasawa T, Kawashima Y, Ishikawa I. Papillon-Lefèvre syndrome: Serum immunoglobulin G (IgG) subclass antibody response to periopathic bacteria - A case report. J Periodontol., 2001; 72: 1747-1754.
20. Lundgren T, Renvert S, Papapanou PN, Dahlén G. Subgingival microbial profile of Papillon-Lefèvre patients assessed by DNA probes. J Clin Periodontol., 1998; 25: 624-629.
21. Robertsson KL, Drucker DB, James J, Blinkhorn AS, Hamlet S, Bird PS. A microbiological study of Papillon-Lefèvre syndrome in two patients. J Clin Pathol., 2001; 54: 371-376.
22. Rateitschak Pluss EM, Schroeder HE. History of periodontitis in a child with

Papillon Lefevre syndrome: A case report. J Periodontol., 1984; 55: 35-46.
23. Shapira J, Eidelman E, Fuks A, Hacham-Zadeh S. Treatment of Papillon Lefevre syndrome with chemotherapy: Report of cases. Spec Care Dentist, 1985; 5: 71 4.
24. Lundgren T, Renvert S. Periodontal treatment of patients with Papillon Lefevre syndrome: A 3 year follow-up. J Clin Periodontol., 2004; 31: 933-8.
25. Ullbro C, Crossner CG, Lundgren T, Stålblad PA, Renvert S. Osseointegrated implants in a patient with Papillon Lefevre syndrome. A 4 ½ year follow up. J Clin Periodontol., 2000; 27: 951-4.
26. Gelmetti C, Nazzaro V, Cerri D, Fracasso L. Long term preservation of permanent teeth in a patient with Papillon Lefevre syndrome treated with etretinate. Pediatr Dermatol., 1989; 6: 222-5.
27. De Vree H, Steenackers K, De Boever JA. Periodontal treatment of rapid progressive periodontitis in 2 siblings with Papillon Lefevre syndrome: 15 year follow up. J Clin Periodontol., 2000; 27: 354-60.
28. Eickholz P, Kugel B, Pohl S, Näher H, Staehle HJ. Combined mechanical and antibiotic periodontal therapy in a case of Papillon Lefevre syndrome. J Periodontol., 2001; 72: 542-9.