Papillon Lefèvre Syndrome: A Case Report and Review of Etiopathogenesis

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Abstract: Papillon Lefèvre syndrome (PLS) is a very rare autosomal recessive disorder characterised by palmar-plantar hyperkeratosis and early onset periodontitis, leading to premature loss of both primary and permanent dentitions. Patients also have increased susceptibility to infections as manifested by association with liver abscess. Genetic studies have shown that the mutations of cathepsin C gene are responsible for this syndrome. Cathepsin C is an enzyme which processes and activates several granule serine proteinases critical to immune and inflammatory responses of myeloid and lymphoid cells. The other factors playing a role in pathogenesis of PLS include parental consanguinity and alteration of host defence. A case of PLS is presented with patient having characteristic lesions on the skin of palms and soles and edentulous upper and lower dental arches. Also, the etiopathogenesis of this less understood syndrome is reviewed. [Dipti T NJIRM 2016; 7(6): 114-116]

Key-words: Cathepsin C, Papillon Lefèvre syndrome, Periodontitis

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Introduction: Papillon Lefèvre syndrome (PLS) is a rare autosomal recessive genodermatoses which was first described by Papillon and Lefèvre in 1924. It is characterized by hyperkeratosis of the palms and soles and severe early onset periodontitis that results in the premature loss of teeth. This disease usually has its onset between the ages of 1 and 4 and affects males and females with equal frequency. Its prevalence is estimated to be 1 to 4 per million in the general population with carrier rate of 2 to 4 per 1000.[1] In addition to the cardinal features, some PLS patients are reported to have an increased susceptibility to infections.[2]

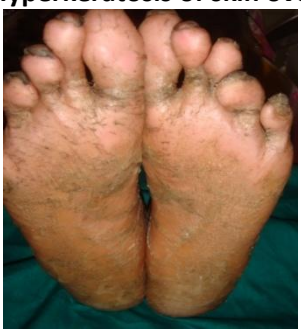
Here, a case of PLS is presented and the etiopathogenesis of this less understood palmoplantar keratoderma is reviewed.

Case Report: A 32 year old female patient reported for replacement of her missing teeth. She was the child of healthy non-consanguineously married parents. The past medical history revealed presence of skin lesions which started developing by the age of six months. The patient reported cycles of exacerbation and remission of the skin lesions. None of her siblings suffered from similar condition.

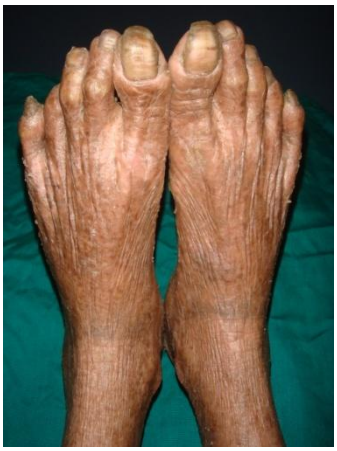
Dermatological examination revealed increased keratinisation of the skin of the palmar and plantar surfaces (figure 1). Skin of both palms and soles was peeling off, suggestive of keratoderma. The hyperkeratinised skin was clearly demarcated from adjacent normal skin. Deep fissures were present on the palms. There was associated hyperhidrosis of palms and soles. The lesions also involved the skin over the dorsal surfaces of the forearms extending up to elbow joint as well as the dorsal surface of feet (figure 2) and parts of legs below the knee joint. There was dystrophy and transverse grooving of the nails. The hair appeared normal.

Extra-oral examination revealed reduced vertical dimension of face. The past dental history revealed that the deciduous teeth had erupted normally, but there had been early shedding, starting at age of 3 years and complete shedding of all deciduous teeth occurred by the age of 6 years. There had been normal eruption of all permanent teeth, but gradually the teeth started becoming mobile and this was followed by exfoliation of teeth. All the permanent teeth were exfoliated by the age of 15-16 years. Intraoral examination revealed edentulous upper (figure 3) and lower (figure 4) dental arches. On the basis of clinical features diagnosis of Papillon Lefèvre syndrome was made. For treatment of cutaneous lesions, the patient was referred to a dermatologist and was prescribed topical keratolytic preparation containing 20% salicylic acid. For her edentulous upper and lower dental arches, complete dentures were fabricated.

Fig: 1: Hyperkeratosis of skin over soles



Fig; 2: Hyperkeratosis of skin over dorsal surface of feet



Fig; 3: Edentulous upper dental arch

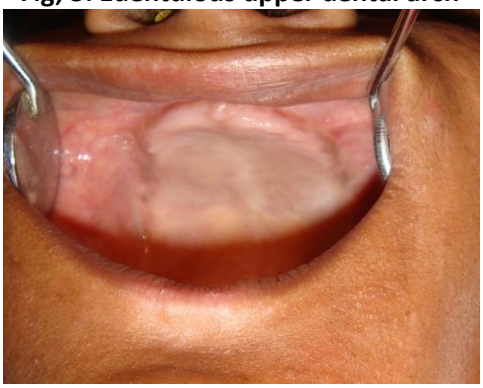
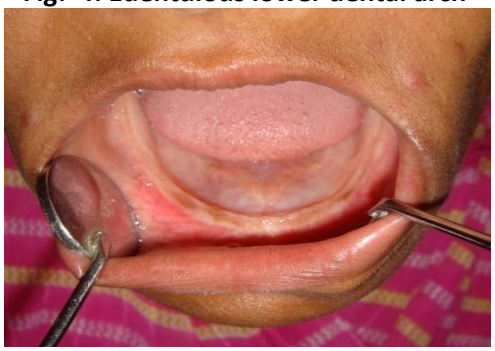


Fig: 4: Edentulous lower dental arch



Discussion: Etiopathogenesis of PLS: PLS is inherited as an autosomal recessive disorder. The postulated underlying mechanisms are mutation of the gene encoding for cathepsin C, immune alterations, alterations in the gingival tissues and the presence of Actinobacillus actinomycetemcomitans.

Consanguinity: Parental consanguinity has been demonstrated in 20–40% of cases of PLS.[1] Consanguineous marriage is a cultural practice with ancient roots, and 20% of the world's population currently lives in communities that prefer this form of marriage.[3] In the present case there is no history of consanguineous marriage.

Role of Cathepsin C: PLS is reported to be due to mutations in the CTSC gene encoding cathepsin C, a lysosomal cysteine protease also known as dipeptidyl peptidase I.[4,5] Cathepsin C is expressed at high levels in lung, kidney, placenta, palms, soles, knees, gingiva, inflammatory cells such as neutrophils, alveolar macrophages, mast cells, and cytotoxic lymphocytes.[4] Cathepsin C is shown to have a role in general protein degradation and turnover.[6] It is also involved in immune and inflammatory responses that include the activation of phagocytic cells and T-lymphocytes, leading to the final elimination of pathogens. Therefore, inactivation of the cathepsin C due to mutations result in the blocking of these responses leading to infection of gingiva and surrounding tissues by pathogens, ultimately leading to tooth loss. Alternatively, cathepsin C might influence periodontal disease progression through its role in epithelial differentiation or desquamation. Since the sulcular and junctional epithelium of gingiva represent the first line of defence against pathogens, their aberrant differentiation due to mutant CTSC gene may alter the mechanical barrier to periodontal pathogens.[7]

Role of Bacteria: Microbiological studies in PLS patients have shown presence of a complex subgingival flora including recognised periodontal pathogens such as A actinomycetemcomitans and F nucleatum.[8] The relatively high prevalence of A. actinomycetemcomitans indicates that PLS patients may have serious trouble in coping with this bacterium.[9]

Alteration of Host Defence: Cathepsin C is the activator of the PMN derived serine proteinases-elastase, cathepsin G and proteinase 3. These proteinases, together with antimicrobial peptides (e.g. LL-37), form the basis of the oxygen-independent machinery used by PMNs to kill bacteria. Also, the PMNs of PLS patients are unable to degrade the leukotoxin of A. actinomycetemcomitans, which is the prime virulence factor for this pathogen.[9] Studies have also shown reduced response of neutrophil function test to Staphylococcus spp. and A. actinomycetemcomitans in PLS.[10]

Another consistent immune dysfunction observed in PLS is impairment of natural killer cell cytotoxic

function, which might contribute to the development of periodontitis.[10]

Association with Liver Abscess: Patients with PLS are predisposed to develop pyogenic liver abscess. Bacteremia during periods of extensive periodontal inflammation associated with the abnormal polymorphonuclear chemotaxis and oxygen consumption are known to occur in PLS. These two factors likely contribute to the development of the liver abscess.[2]

Conclusion: In summary, PLS is a rare autosomal recessive disorder. There is altered response of host to various pathogens due to absence of cathepsin C activity leading to the manifestations of the disease. The complex etiopathogenesis of PLS means that successful management of this syndrome remains challenging. As our understanding of the etiologic factors increases, it is hoped that better treatment modalities can be developed for this syndrome.

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