Partial Expression of the Papillon-Lefevre Syndrome
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ABSTRACT
Papillon-Lefevre Syndrome (PLS) is a rare autosomal recessive genodermatosis characterized by palmar-plantar hyperkeratosis, and destructive periodontitis. It is transmitted with an estimated frequency of one to four per million individuals. The two hallmarks of the syndrome, dermatological lesions and destructive periodontitis, are known to occur as independent diseases. We present a unique case of Papillon-Lefevre syndrome in a 28 years old woman with its pathognomonic dermatological features without oral features.

Key Words: Papillon-Lefevre Syndrome. Palmar-plantar hyperkeratosis. Palmoplantar keratoderma.

INTRODUCTION
Papillon-Lefevre Syndrome (PLS) was first described by two French physicians M.M. Papillon and Paul Lefevre in 1924 as a condition characterized by hyperkeratosis of the palms and soles combined with severe periodontitis, leading to premature loss of deciduous and permanent dentition.1 It is a rare autosomal recessive disorder, attributed to a point mutation of the cathepsin C gene, transmitted with an estimated frequency of one to four per million individuals.2 Because of increased awareness of the disease, mainly dentists have diagnosed over half of the reported cases. The two major components of the syndrome, dermatological lesions and destructive periodontitis, are known to occur as independent entities.3

Here we are reporting a case of a 28 years old woman with typical dermatological features of Papillon-Lefevre syndrome.

CASE REPORT
A 28 years old lady reported with an abnormal thickening of her palms and soles, which her parents noticed within few months after her birth. It started as a small macular lesion on the palm, which was followed by similar lesion on the sole, later on progressed to involve the entire palm and sole surfaces. These lesions were asymptomatic regardless of excessive sweating of the palms, multiple fissures on the interphalangeal joints and dry, scaly lesions on the knees and elbows, which was more pronounced in the winter season. She was the third child of non-consanguineous, healthy parents. Pregnancy was uncomplicated. Parents were in their 3rd decade of life at the time of child birth, with maternal age of 28 years. Delivery was full term and normal, birth weight was 2800 g. All the milestones of childhood were normal. Eruption of both dentition and exfoliation of deciduous dentition followed normal physiological pattern. Her two elder female siblings were normal.

On general examination, the patient had overall normal physical and mental development. Examination of hands and feet showed presence of distinguishable hyperkeratosis bilaterally over the entire palms, soles and knees, with multiple fissures on the interphalangeal joints (Figures 1A and 1C). Discrete psoriasiform lesions were present on the elbows, dorsal aspect of the hands and ventral aspect of the wrists. The nails were of abnormal shape with prominent horizontal ridges (Figure 1B). On intraoral examination, there were no signs of periodontal pathology (Figure 2). Panoramic radiography revealed no signs of periodontal bone destruction (Figure 3A). Lateral skull projection showed no evidence of intracranial calcifications (Figure 3B). Laboratory investigation regarding neutrophilic function revealed normal respiratory burst and intracellular killing activities; however, chemotactic and phagocytic

Figure 1: (A) Hyperkeratosis of the palms with multiple fissures on the interphalangeal joints; psoriasiform lesion on the ventral aspect of the wrists. (B) Psoriasiform lesions on the dorsal aspect of the hands; abnormal shaped nails with prominent horizontal ridges. (C) Hyperkeratosis of the soles.
activities were found to be defective. Based on the above mentioned clinical features and investigations, the case was diagnosed as Papillon-Lefevre syndrome with its partial expression.

DISCUSSION

The Papillon-Lefevre Syndrome (PLS) is a rare genodermatosis manifesting as palmar plantar hyperkeratosis with severe periodontitis. Recently, a few research groups have reported that mutations of the lysosomal proteases, cathepsin C, gene mapped on chromosome 11q14-q21, is associated with PLS. This particular gene is expressed in the epithelial regions commonly affected by PLS, such as soles, palms, knees, gingiva and also various immune cells, including polymorphonuclear leukocytes, macrophages and their precursors. In the present case, PLS was suspected because of clinical signs and symptoms. In 1979, Hanke proposed the following three criteria to classify a case as PLS: autosomal recessive inheritance, palmar plantar hyperkeratosis, precocious loss of primary and permanent teeth. This case can be considered as having an autosomal recessive inheritance as both parents were phenotypically healthy and other two siblings were not affected.

The severity of Palmoplantar Keratoderma (PPK) is variable. The typical lesion has its onset between the ages of 1 and 4 years. The sharply demarcated keratotic plaques may occur focally, but usually involve the entire surface of the palms and soles, sometimes extending onto the dorsal surface of the hands and feet. The lesions are usually diffuse and punctate, with dry scaly skin which vary in thickness from one to several millimeters. A foul smell maybe associated due to hyperhidrosis of the palms and soles. The psoriasiform plaques may also be seen on the knees and elbows. The lesion of the plantar surface extends to the edges of the soles and occasionally onto the skin overlying the external malleoli and achilles tendon. The hair is usually normal, but in advanced cases the nails may show transverse grooving and fissuring. These symptoms may get worsen in the winter and associated with painful fissures. All these features were consistent with the present case. However, the feature of aggressive periodontitis were absent in this case.

Mental retardation, increased susceptibility to infections of internal organs, such as of liver, lung, kidney, asymptomatic calcification of the falx cerebri and choroid plexus have been noted as additional features in many PLS patients. These rare findings could be due to the result of a high degree of homozygosity at other alleles in addition to cathepsin C locus. None of these findings were observed in this case.

Some of the other conditions where patients present with palmar plantar hyperkeratosis without the involvement of periodontium are palmoplantar keratoderma of Unna-Thost, Howel-Evans syndrome, Vohwinkel syndrome and Greither syndrome. PPK of Unna-Thost shows waxy or verrucous, yellowish white symmetric hyperkeratosis. Howel-Evans syndrome is associated with development of esophageal carcinoma. In Vohwinkel syndrome, the PPK shows a diffuse honeycomb pattern. Additional features include starfish-shaped keratotic plaques on dorsal hands, feet, elbows, and knees as well as constricting digital bands, which may progress to autoamputation. Greither syndrome shows symmetrical telangiectasia. All these conditions were excluded because none of these features were present in this case.

The skin manifestations are treated with emollients with salicylic acid (topical keratolytic) and urea added to enhance the effect. Oral retinoids including isotretinoin, acitretin and etretinate are the mainstay of treatment for the keratoderma associated with PLS. Topical steroids, with or without keratolytics, can be considered in those conditions where there is an inflammatory component. Regular foot care, careful selection of footwear, and treatment of fungal infections are mandatory. Dermabrasion may help topical agents penetrate; while carbon dioxide laser treatment may be beneficial in limited conditions. For severe cases, total excision of hyperkeratotic skin followed by grafts may need to be considered.
Both the hallmarks of PLS (PPK and periodontal disease) can occur as an independent diseases. So, the question is, does PLS represent a multi-genetic disease with co-expression of two closely linked loci or variable clinical expression of a single gene defect? Variable clinical expression of single gene mutations is possible due to the interaction between a disease gene and other modifying genes. This could result in partial expression of this syndrome. On the other hand, majority of the Papillon-Lefevre syndrome cases feature dermatological as well as periodontal findings, where collaboration between the dermatologist and the dentist may be required for proper diagnosis and the management.

REFERENCES


