

Papillon-Lefevre syndrome: case report

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Abstract

Papillon-Lefevre syndrome (PLS) is a rare genodermatosis of autosomal recessive inheritance manifesting as palmoplantar hyperkeratosis with periodontitis. A 4-year old Iranian girl was referred to the Mazandaran University Hospital, Sari complaining of well-demarcated, psoriasiform, yellowish, keratotic plaques over the skin of her palms and soles with transgrediens. For cutaneous lesions, she was treated with oral acitretin 0.5 mg/kg/day and topical keratolytic 5% salicylic acid in combination with 10% urea.

Key words

Papillon-Lefevre syndrome.

Introduction

Papillon-Lefevre syndrome (PLS) is a rare genodermatosis of autosomal recessive inheritance manifesting as palmar and plantar hyperkeratosis with periodontitis.¹ It was first described by two French physicians, Papillon and Lefevre, in 1924.^{2,3}

The disorder is first seen in children in the age group of 1-4 years. No racial or sexual predilection is reported. A genetic predisposition, however, exists with greater frequency of occurrence in the consanguineous offspring.^{2,4} Genetic, immunologic and microbiologic factors are suggested as responsible for the initiation and progression of the disease. Genetic studies have shown that mutations in the major gene locus of chromosome 11q14 with loss of function of the cathepsin C gene are responsible for PLS.^{5,6} Studies in PLS patients have shown more than 90% reduction in cathepsin C activity.⁷ Another important etiologic factor is an alteration of host defence owing to the

decreased function of lymphocytes, polymorphonuclear leukocytes (PMNs), or monocytes.⁸

Characteristic clinical features are diffuse palmoplantar keratoderma, premature loss of deciduous and permanent teeth and a tendency to recurrent pyogenic infections of the skin.⁹ The erythematous keratotic plaques may be focal or diffuse and are characterized by transgradient extension of keratoderma to the dorsal surface of palms and soles. Well-demarcated psoriasiform plaques usually occur on knees and elbows. Repeated episodes of periodontitis and gingivitis lead to destruction of periodontium and subsequent premature loss of deciduous and permanent teeth.¹⁰ We presents a brief overview of PLS and describe the clinical presentations in a case with typical dental and dermatological findings.

Case Report

A 4-year old Iranian girl was referred to the Mazandaran University Hospital at Sari complaining of well-demarcated, psoriasiform, yellowish, keratotic plaques over the skin of her palms and soles with transgrediens. Also the lesions could be seen on the elbows, knees and dorsal surface of the legs (**Figure 1, 2**).

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Figure 1 Well-demarcated, psoriasiform, yellowish, keratotic plaques over the skin of her palm and soles with transgredient.



Figure 2 Palmar keratoderma.



Figure 3 Loss of teeth



Figure 4 After 2 month treatment with oral acitretin 0.5 mg/kg/day.

The patient was moderately built with a steady gait. Her physical and mental development was also normal. Except for a slight articulatory defect, her speech was normal and she had the ability to comprehend and communicate satisfactorily. Cutaneous examination revealed dry skin with normal development of hair and nails. There were symmetric, well-demarcated, yellowish, keratotic, and confluent plaques with adherent scales, affecting the skin of her palms and soles, also extending onto the dorsal surfaces of hands and feet (transgrediens). Intraoral examination showed premature loss of teeth. There was no active inflammation of the gum. No other abnormality was detected in relation to soft tissue (**Figure 3**). Patient had a reduced facial height due to resorption of the alveolar ridge.

Hematological investigations were normal. Biochemical profile including liver function tests and lipid profile were carried out and were found to be within the normative range of values. Histopathology examination of a skin biopsy specimen from the hyperkeratotic area showed non-specific changes, with orthohyperkeratosis, acanthosis, and a reduction or thickening of the granular cell layer.

Based on clinical findings a diagnosis of PLS was established in this patient. For cutaneous lesions, she was treated with oral acitretin 0.5 mg/kg/day and topical keratolytic 5% salicylic acid in combination with 10% urea (**Figure 4**).

Discussion

Papillon-Lefevre syndrome was first described by two French physicians, Papillon and Lefevre in 1924.¹¹ This is an extremely rare disease with a prevalence of 1-4 cases per million. Males and females are equally affected and there is no racial predominance.¹² The disorder is first seen in children in the age group of 1-4 years.^{2,4} The present patient was 4 years old when she first visited the Mazandaran University Hospital at Sari.

Although the exact pathogenesis of this syndrome remains relatively obscure, immunologic, microbiologic, and genetic basis have been proposed. Microbiological studies have demonstrated *Actinobacillus actinomycetemcomitans*, *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, and *Treponema denticola* organisms, suggesting that many pathogens may be involved in the disease process.¹³ Previous case reports and studies have reported that *A. actinomycetemcomitans* plays a significant role in the pathogenesis and progression of the rapid periodontal breakdown seen in PLS.^{7-10,14,15}

The inheritance is autosomal recessive and the point of mutation is the gene for cathepsin C (CTCS), a lysosomal protease, which lies on chromosome (11q14-q21).^{16,17} In this case, genetic testing could not be performed to identify the gene mutation because of the low economic status of the guardians, but the dermatological, dental findings and paraclinical features strongly suggested the diagnosis of PLS.

The dermatological lesions appear first between the ages of 1 to 4 years and include

palmoplantar keratosis, varying from mild psoriasiform scaly skin to overt hyperkeratosis. The lesions may be aggravated by cold.¹⁸ This 4 year old patient, exhibited well-demarcated, psoriasiform, yellowish, keratotic plaques over the skin of her palm and soles with transgredient.

Nail changes are apparent in advanced cases and are manifested by transverse grooving and ridging.¹⁹ In our patient nail changes were not present.

About 20% patients with Papillon-Lefevre syndrome have an increased susceptibility to infections due to some dysfunction of the immune system.²⁰⁻²²

Many interesting case reports of this uncommon hereditary disorder have been published from different parts of the world from time to time, with various associations such as liver abscess, ectopic intracranial calcification, hyperhidrosis, hypertension, hyperglycemia, thyroid enlargement, osteoporosis and congenital hydrocele, etc.²³ Pyogenic liver abscess is recognized to be a fairly frequent complication of Papillon-Lefevre syndrome. The case presented here, however, did not demonstrate any abnormal liver function.

The other features of PLS are the intracranial calcification of choroid plexus and tentorium on radiographic examination and palmoplantar hyperhidrosis. These were not present in our patient.²⁴

To date, only two cases of PLS associated with malignant cutaneous neoplasms, both malignant melanomas have been reported in the literature, in a Jew and Japanese.^{25,26} It has been reported that no association with malignant neoplasms, including malignant melanoma, was observed in 120 cases of PLS.²⁷

The management of cases with PLS requires a multidisciplinary approach with the active participation of the dental surgeon, dermatologist and pediatrician.

The differential diagnoses include Haim-Munk syndrome and hypophosphatasia. Haim-Munk syndrome also exhibits arachnodactyly, acroosteolysis, atrophy of nails, and deformity of the phalanges in the hands. None of these features were found in the present case. In hypophosphatasia, deficiency of alkaline phosphatase activity is seen,²⁸ but in our cases the values were within normal limits and therefore this differential diagnosis could be excluded.

Conclusion

Even though PLS is extremely rare condition it is associated with lifelong psychological and social impact on growing children. Patients diagnosed with PLS suffer from its adverse effects throughout adolescence. They may have symptoms of depression, including hopelessness, aimlessness, social phobia, and a fear of communicating with people outside their family. Combined cooperation from dermatologists, pediatrician, and prosthodontists is critical for the overall care of patients suffering from PLS.

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