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Papillon-Lefevre Syndrome

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Abstract

Background: Papillon-Lefevre syndrome is a rare autosomal recessive disorder caused by cathepsin C gene mutation leading to the deficiency of cathepsin C enzymatic activity. The disease is characterized by palmoplantar hyperkeratosis, loss of deciduous and permanent teeth and increased susceptibility to infections. Onset of palmoplantar hyperkeratosis and periodontopathy is most commonly before the age of 4 years.

Main observations: A 15 year old boy with a history of frequent infections presented with hyperkeratosis of palms and soles, which worsened during winter season. Examination of the oral cavity revealed missing mandibular central incisors and left lateral incisors. Most remaining permanent teeth were mobile. Fibrosis and scarring of gingival and labial mucosa restricted opening of the mouth.

Conclusion: Early diagnosis of Papillon-Lefevre syndrome may help preserve the teeth. We present a case of a late diagnosis of this syndrome.

Introduction

Papillon-Lefevre syndrome is an extremely rare genodermatosis inherited as an autosomal recessive trait. The disease is caused most coomonly by Cathepsin C gene mutations leading to the deficiency of cathepsin C enzymatic activity.[1,2] Characteristic clinical features are: diffuse palmoplantar keratoderma, premature loss of deciduous and permanent teeth and a tendency to recurrent pyogenic infections of the skin. Palmoplantar hyperkeratosis typically starts between 1-4 years of age.[3] 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 knee and elbows.[4] Repeated episodes of periodontitis and gingivitis lead to destruction of periodontium and subsequent premature loss of deciduous and permanent teeth.[4] In addition to palmoplantar hyperkeratosis and oral findings, patient may have impaired function of the immunological system, associated most probably with insufficiency of cathepsin C, which is essential for granzyme B activation and NK cell cytolytic activity.[5,6] These abnormalities are associated with increased susceptibility to recurrent pyogenic infection of skin.[4]

Case report

A 15 year old boy presented with persistent thickening and scaling of skin of palms and soles, which worsened during winter season. There was history of frequent infections of skin over trunk and extremities and recurrent swelling of gums, foul breath and loss of teeth. There was no history of excessive sweating. There was history of parental consanguinity. The patient's siblings were healthy.

General physical and systemic examination was within normal limits. Cutaneous examination revealed symmetrical diffuse hyperkeratosis and mild erythema affecting the skin of palms and soles extending to the dorsal surface of hands and feet (Fig. 1A). There were well defined circumscribed psoriasiform plaques on knees bilaterally. Examination of the oral cavity revealed missing mandibular central incisors and left lateral incisors (Fig. 1B). There was no active inflammation of the gums but there was fibrosis and scarring of gingival and labial mucosa which restricted opening of the mouth. The remaining permanent teeth were mobile except for the upper and lower molars. There was marked atrophic scarring at the sites of infection on trunk and scalp (Fig. 1C, 1D). Nails were normal on examination. Complete blood count, liver function tests and kidney function tests were normal. X-ray skull was

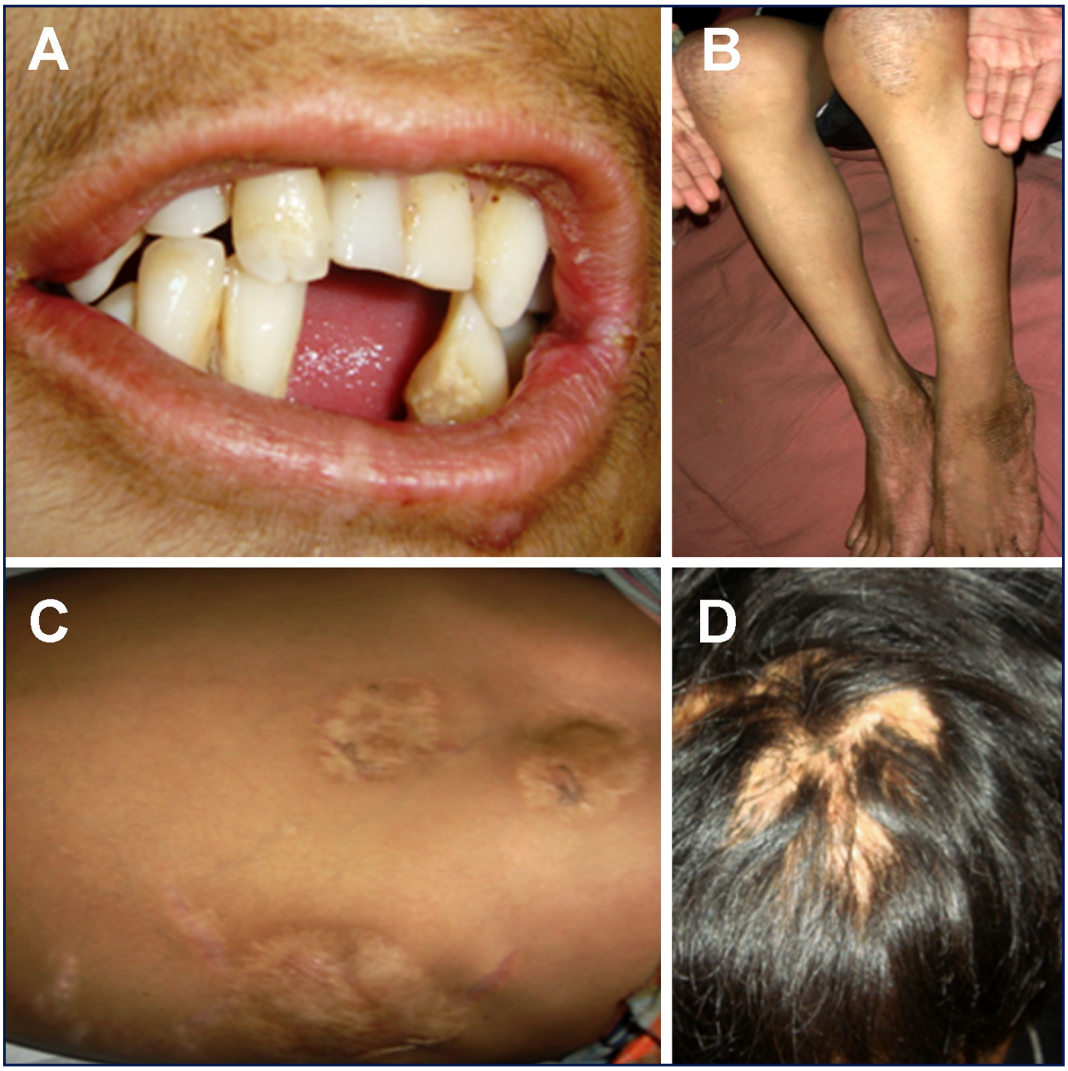

Figure 1

Patient with Papillon-Lefevre Syndrome.
Loss of permanent dentition (A), hyperkeratosis of dorsal aspect of feet and palms and psoriasiform plaques on knees (B). Atrophic scarring resulting from recurrent Infections on the trunk (C) and scalp (D).

normal. The X-ray of mandible revealed resorption of alveolar bone. Histopathology examination of a skin biopsy specimen from the hyperkeratotic area showed hyperkeratosis, parakeratosis, acanthosis and perivascular infiltrate in dermal papillae. Based on clinical findings a diagnosis of Papillon-Lefevre syndrome was established in this patient.

Discussion

Papillon-Lefevre syndrome was first described by two French physicians, Papillon and Lefevre in 1924.[7] This is an extremely rare disease with a prevalence of 1-4 cases per million.[8] Males and females are equally affected and there is no racial predominance.[8] 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).[2,9] The mutation of this gene leads to total loss of cathepsin C activity in patients and reduced activity in obligate carriers. Normally, the gene is expressed predominantly in epithelial regions affected in Papillon-Lefevre syndrome such as palms, soles, gingiva and immune cells and their precursors.[10]

Palmoplantar keratoderma typically starts between 1-4 years of age and it extends in a transgradient pattern with sharply demarcated borders. The symptoms may worsen in winter and may result in painful fissures.[4] The periodontitis starts at the age of 3-4 years after the normal eruption of deciduous teeth.[4] The subsequent destruction of periodontium results in premature loss of deciduous teeth by the age of 4 years. This process of gingivitis and periodontitis is repeated again after the eruption of permanent teeth and leads to premature loss of permanent dentition.[4] Nail changes are apparent in advanced cases and are manifested by transverse grooving and ridging.[11] 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.[5,12,13]

Most common are recurrent skin infections. In our patient there was history of repeated cutaneous infections which led to scarring alopecia on scalp and areas of atropic scarring on trunk. Almuneef *et al* 2003[13] have described pyogenic liver abcess as a common complication in Papillon-Lefevre syndrome patients. A similar case of pyogenic liver abscess was described by Tanaka *et al* in 2008.[12]

The other features of Papillon-Lefevre syndrome are the

intracranial calcification of choroid plexus and tentorium on radiographic examination and palmoplanter hyperhidrosis.[14] These were not present in our patient.

Two close differential diagnoses of Papillon-Lefevre syndrome are Haim Munk Syndrome[15] and prepubertal periodontitis.[16,17] Haims-Munk syndrome is an allelic variant of Papillon-Lefevre syndrome and the clinical features, in addition to palmoplanter keratoderma and loss of dentition, include arachnodactyly (claw like phalanges with convex nails), and acroosteolysis.[15] In prepubertal periodontitis palmoplanter hyperkeratosis is absent.[16] Oral retinoids including acitretin, etretinate and isotretinion combined with intensive antimicrobial treatment are the mainstay of treatment in Papillon-Lefevre syndrome.[2,18,19] It should be considered to start treatment at eruption of the first teeth and maintain therapy during the development of permanent teeth.[19]

Early diagnosis of Papillon-Lefevre syndrome and appropriate treatment may help to prevent of loss of dentition in these patients.

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