

Case Report

Successful Treatment of Papillon Lefèvre Syndrome with a Combination of Acitretin and Topical-PUVA; A Four Year Follow Up

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Abstract

Observations: *Papillon-Lefèvre Syndrome* (PLS) is a rare autosomal recessive disorder characterized by palmoplantar hyperkeratosis, periodontitis which causes premature loss of both deciduous and permanent teeth and recurrent pyogenic infections. Topical keratolytics, antibiotics and retinoids, such as isotretinoin and acitretin, have been used in the treatment of PLS. We report a 5 years old girl with palmoplantar hyperkeratosis and chronic eye infection persisting over 1,5 years. She also defined recurrent skin lesions which began as purple lesions that evolved into abscesses and finally healed with scars on her hips, trunk and scalp. All deciduous teeth were previously lost due to chronic swelling and bleeding of the gums, except for two molars. Acitretin (10 mg/day) in combination with topical-PUVA therapy twice weekly was initiated. Additionally, she also used keratolytic preparation containing 5% salicylic acid in 10% urea and pure vaseline for palmoplantar hyperkeratosis. An improvement on the palmoplantar hyperkeratosis and chronic eye infection was observed after 4 sessions of topical PUVA therapy and within 6 weeks of therapy respectively. Four months after initiating treatment with acitretin, she had new permanent teeth.

Introduction

Papillon-Lefèvre Syndrome (PLS) is a rare autosomal recessive disorder characterized by diffuse, transgradient palmoplantar keratoderma (PPK), destructive periodontitis beginning in childhood, premature loss of teeth, frequent cutaneous and systemic pyogenic infection [1]. The prevalence of PLS has been reported as 1 to 4 per million population [2]. We describe the successful use of the acitretin and local-PUVA combination therapies in a child who had new permanent teeth and significant improvement in her chronic skin infection with this therapy.

Case Report

A 5-year-old girl presented with hyperkeratosis and fissures on palmoplantar surfaces extending from the age of 3 years. Her parents noted that she had recurrent abscesses healing with scars since early infancy. She had lost all her deciduous teeth due to chronic swelling and bleeding of the gums until the age of 2 years. She had no family history of similar dermatological findings. Her parents were third cousin.

On dermatological examination there were multiple fissured erythematous hyperkeratotic plaques on the soles. Xerosis and erythema on the palms and dispersed erythematous papules on the trunk. There were also multiple scars in variable sizes on the preauricular, occipital and gluteal re-



Figure 1. Fissured hyperkeratosis on the soles

gions. Oral examination revealed complete loss of the deciduous teeth, except for two molars (**Figures 1 and 2**).

Laboratory investigations including complete blood count, transaminase, lipid profile, glucose, albumin, bilirubin, urinalysis (chemical, microscopic) were within normal range. Her serologic screens were negative for VDRL, HbsAg, anti-HBS, anti-HCV, and anti-HIV.

Abdominal, thoracic and cranial computerized tomography examinations to assess the intraabdominal and intrathoracic abscess and intracranial calcifications revealed no abnormalities. Panoramic dental radiograph demonstrated loss of teeth.

Histopathological examination of erythematous-squamous plaques revealed orthokeratotic type hyperkeratosis, acanthosis, loss of stratum granulosum and minimal dermal perivascular mononuclear infiltration.

Topical keratolytic 5% salicylic acid in combination with 10% urea treatment and systemic in combination with topical 8-methoxypsoralen-ultraviolet A phototherapy acitretin (10 mg/day) (PUVA) were initiated.

New permanent teeth appeared four months after the initiation of therapy (**Figure 3**). Five months after cessation of therapy her symptoms reappeared and acitretin 10 mg/day in combination with topical PUVA restarted. At the 8th session of therapy marked retinoid dermatitis presenting as a diffuse, scaly, pruritic erythema on the gluteal region and extremities was observed. Acitretin was stopped and therapy continued with topical PUVA alone. The palmoplantar lesions were cleared after 38 sessions, with a total



Figure 2. Multiple scars on the gluteal region of 118 joules/cm².

In summary, the patient was lesion free at the 8th session with combination therapy and at 38th session with topical PUVA alone.

Discussion

The inherited PPK constitutes a complex heterogeneous group of disorders characterized by thickening of the palms and the soles. PPK have been classified into three groups: diffuse, focal, punctuated. PLS is classified as a diffuse palmoplantar keratoderma associated with ectodermal dysplasia [3].

PLS is characterized by two major components: dermatological and periodontal changes.

Additional features including decreased leukocytes functions and increased sensitivity



Figure 3. New teeth after 7 months of therapy

for infections, calcification of the dura, falx cerebri, tentorium cerebelli, and choroids plexus and intraabdominal abscesses, have been reported [4, 5, 6, 7]. Ullbro et al did not find any significant correlation between the severity of the periodontal infection and the severity of skin involvement [5].

PLS is caused by mutations in the cathepsin C gene on 11q14. However, Pilger et al reported a case of late-onset PLS without cathepsin C gene mutation [4, 8]. Dermatologically well demarcated, erythematous hyperkeratotic plaques that can extend onto the dorsal surfaces are seen on palms and soles, but may also localize on elbows, knees [4].

The differential diagnosis of PLS includes *Haim-Munk* syndrome and psoriasis. According to the clinical and histopathological findings, we suggested the case as PLS, although did not perform cathepsin C gene mutation analysis.

The skin manifestations of PLS are usually treated topically with emollients, keratolytics including salicylic acid and urea. In winter, PPK of PLS can worsen that may necessitate systemic therapy.

Oral retinoids including acitretin, etretinate, isotretinoin have been shown to be effective treatments for the keratoderma seen in PLS.^{5,6,9-11} However Balci et al recently reported that the use of oral retinoids in the treatment of PLS-associated palmo-plantar keratoderma is not curative [12].

The treatment of the periodontal component of PLS is very difficult. Many authors suggested the importance of the professional dental care and the use of prophylactic antibiotics, but usually this procedure is not enough [13, 14]. It has been shown that acitretin therapy is a safe and effective treatment in pediatric cases of inherited keratinization disorders [15]. Oral retinoids plus antibiotics have been reported with good response [16]. The use of oral retinoids for prolonged period is suggested. It seems beneficial drug to prevent loss of permanent teeth in children [11, 13].

Therefore, we decided to use acitretin which was accepted as the mainstay of treatment. Also intermittent topical PUVA treatment was planned for the exacerbations of palmo-

plantar keratoderma. With this therapy a remarkable improvement for all component of PLS was achieved.

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