Two Cases of Interdigital Psoriasis Successfully Treated with Pimecrolimus Cream 1%

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Psoriasis alba (Interdigital psoriasis), first introduced by Waisman1 in 1961, is an atypical form of psoriasis which has an outstanding clinical picture of a white, sodden appearance. Too often the lesions are erroneously presumed to be of fungal origin, inspiring the diagnosis of macerated dermatophytosis or candidiasis, but the lesions fail to demonstrate the fungal element and are therefore resistant to topical and oral anti-fungal agents. The treatment of psoriasis alba is the same as for other forms of intertriginous psoriasis, of which topical corticosteroids and calcipotriene are commonly used. However, psoriasis alba may be resistant to these therapies and shows fast relapse after cessation of treatment, as in other forms of intertriginous psoriasis[1,2]. Pimecrolimus cream 1% (Elidel®); Novartis Pharmaceuticals, East Hanover, NJ) is a nonsteroid, skin selective, topical inflammatory cytokine inhibitor which is specifically developed for the treatment of inflammatory skin diseases[3]. Herein, we present 2 cases of psoriasis alba successfully treated with pimecrolimus cream 1%.
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Key Words: Psoriasis alba, Pimecrolimus cream 1%

INTRODUCTION

Psoriasis alba (interdigital psoriasis) is a type of intertriginous psoriasis which presents as a distinctive opaque interdigital plaque, and whose psoriatic derivation is difficult to perceive when it occurs alone[1]. It mimics fungal infection by its appearance but is resistant to anti-fungal therapy and as a result, patients with psoriasis alba complain of a persistent dermatosis of the feet.

The location of psoriasis in intertriginous areas, including the interdigital spaces, where the skin is thinner and more sensitive to local side effects, poses a unique challenge to treatment[4,5]. Currently, topical steroids are most commonly prescribed, but local side effects such as atrophy of the skin and recurrence after cessation of treatment limit its usage[1]. Calcipotriene can be used as an alternative treatment, but due to skin irritation, dilution of the agent is required. Pimecrolimus cream 1% (Elidel®; Novartis Pharmaceuticals, East Hanover, NJ) is a nonsteroid, topical inflammatory cytokine inhibitor whose efficacy and safety have been demonstrated in patients with intertriginous psoriasis[6] and in psoriasis of the glans penis[7].

Herein, we report two cases of psoriasis alba successfully treated with pimecrolimus cream 1%. No significant side effects or signs of relapse have been observed to date.

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CASE REPORT

Case 1

A 57-year-old man presented with a 15-year history of a slightly pruritic, white plaque in the 3rd interdigital space of the left. foot. Topical and oral

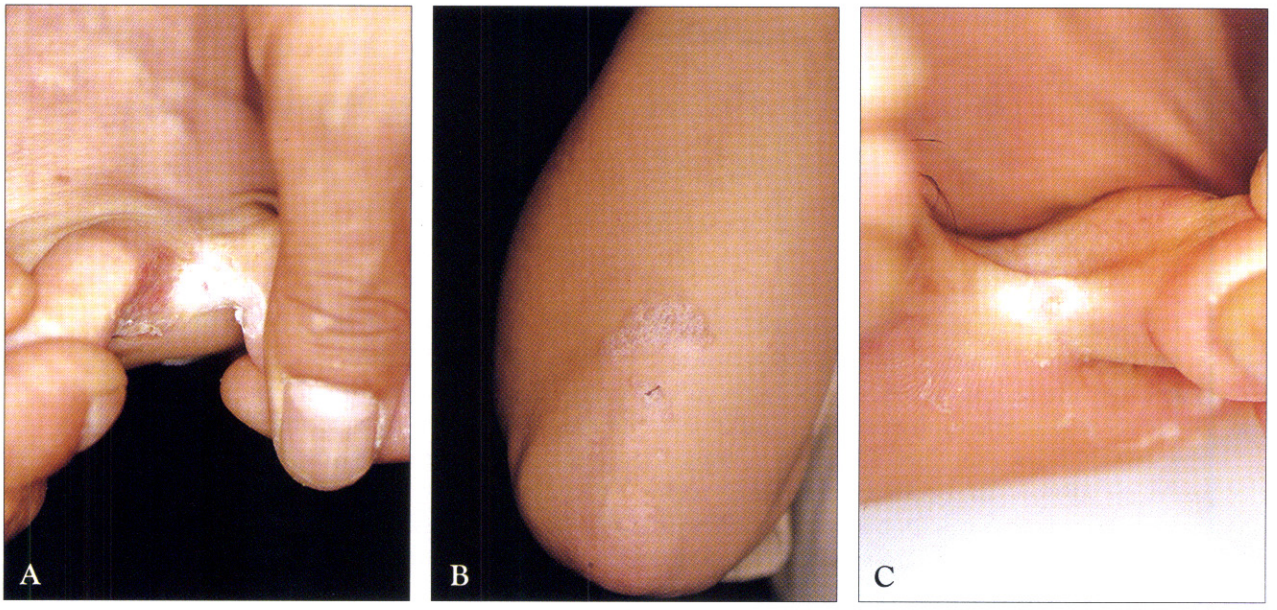

Fig. 1. (A) A whitish patch with a macerated and sodden appearance between the 3rd and 4th digit of the left. foot in patient 1. (B) A concomitant psoriatic scaly plaque on the elbow. (C) Near total disappearance of the lesion after 3 months of treatment in patient 1.

antimycotics were prescribed in adequate doses over several years due to the impression of an interdigital fungal infection, but the lesion had been resistant to therapy.

On physical examination, we noticed a whitish patch with a macerated and sodden appearance between the 3rd and 4th digit of the left Foot (Fig. 1A). No particular odor was detected from the lesion and to our surprise, the lesional skin was quite firm, leathery and pliant. On whole body inspection, multiple, well demarcated, erythematous plaques with adherent thick and silvery white scales were observed on the elbows and buttocks, which had developed 5 years previously (Fig. 1B). The patient had been diagnosed as having psoriasis in another hospital but did not take any oral or topical medication. The KOH examination and fungal culture results from the interdigital space were negative.

A skin biopsy specimen from the interdigital space revealed confluent hyperkeratosis and parakeratosis with perinuclear vacuolization. The stratum granulosum was slightly thinned and the epidermis showed psoriasiform hyperplasia although not as regular as in typical psoriasis (Fig. 2). In the superficial dermis, quite a heavy perivascular infiltrate of lymphocytes were present. The Periodic acid Schiff (PAS) staining was negative, deleting the possibility of a fungal infection. No subcorneal micropustule (Kogoj) or Munro abscess were present. Overall, the histological findings suggested psoriasis, and with the patient's clinical manifestation and a history of having been diagnosed with psoriasis before, we made a diagnosis of psoriasis alba.

Under such diagnosis, we treated the patient with a combination of acitretin (Neotigason®), clobetasol-17-propionate ointment (Dermovate®) and calcipotriol ointment (Diavonex®). The lesions were treated successfully but with cessation of acitretin (Neotigason®), recurrent relapses occurred. The patient also complained of local skin irritation and subjective feelings of skin atrophy which consequently lowered compliance.

As an alternative, we tried topical application of 1% pimecrolimus cream. Significant improvement with a rapid onset time was observed, leading to near total disappearance of the lesion within 3 months of treatment (Fig. 1C). Relapse did not occur and side effects have not been observed.

Case 2

A 45 year-old male was referred to our outpatient department with a 20-year history of persistent white sodden plaques in the 3rd interdigital space of the right foot (Fig. 3A). The patient was an occupational

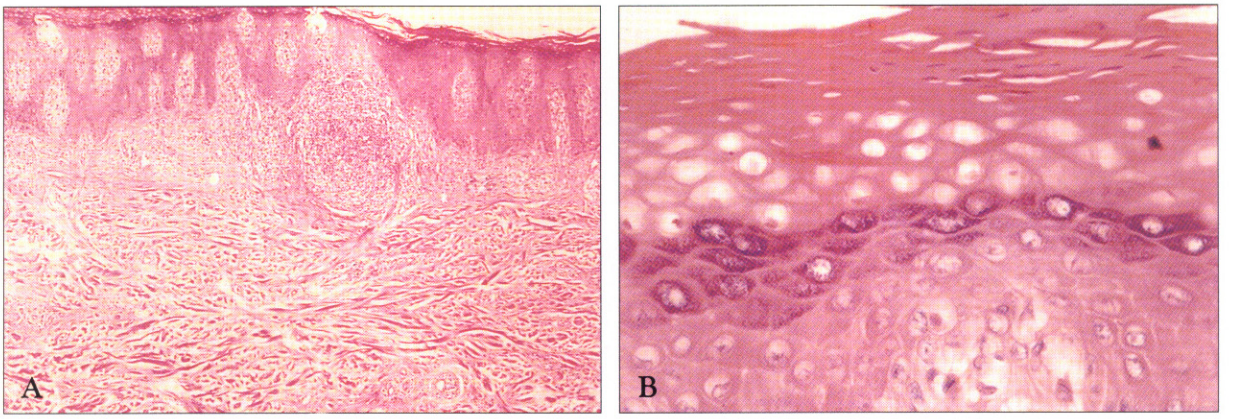

Fig. 2. (A, B) Confluent hyperkeratosis and atypical parakeratosis with perinuclear vacuolization is observed. The epidermis shows psoriasiform hyperplasia, although not as regular as is typical for psoriasis, and the granular layer is nearly intact. In the superficial dermis, a quite heavy perivascular infiltrate of lymphocytes is seen (H-E × 40, × 400).

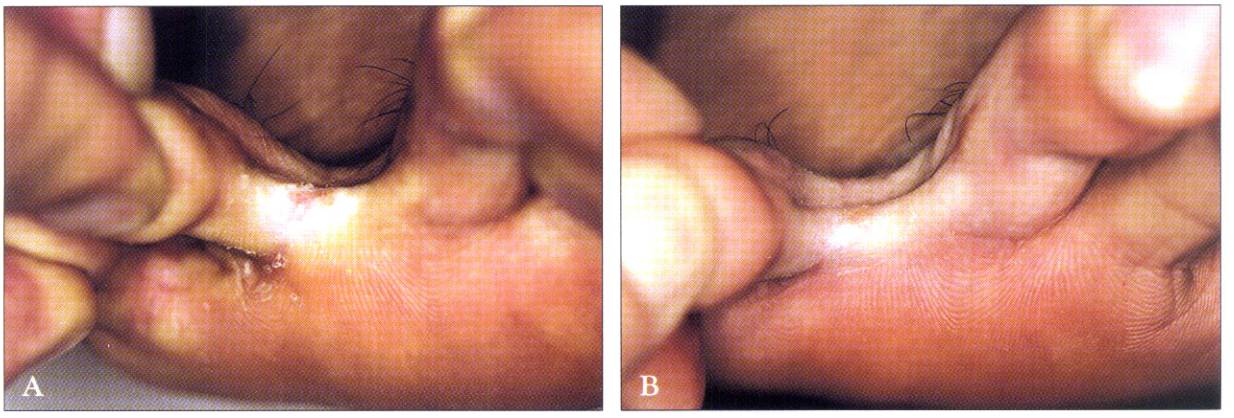

Fig. 3. (A) White sodden plaque in the 3rd interdigital space of the right foot in patient 2. (B) Partial healing of the lesion at the follow up visit, one month after the initiation of 1% pimecrolimus cream in patient 2.

soldier with a history of tinea pedis. Without much doubt, the lesion was considered as an interdigital fungal infection but did not respond to oral or topical anti-fungal agents. The patient had no history of associated illness and on general inspection, no abnormality was found.

For proper diagnosis, a punch biopsy (2 mm) was performed in the interdigital space. The histological findings were very much similar to patient 1, showing hyperkeratosis, atypical parakeratosis with vacuolization, a slightly thin granular layer and significant acanthosis. Special staining with PAS revealed no fungal element, and KOH and fungus culture findings were negative too. Due to the impression of being psoriasis alba, we prescribed 1% pimecrolimus cream for topical application at the lesion site, two times a day. On the follow up visit (one month later), the lesion had improved dramatically (80%) (Fig. 3B). The patient is still undergoing therapy but so far, he has not experienced any irritation or signs of relapse.

DISCUSSION

Occasionally, dermatologists are confronted by patients with persistent interdigital dermatosis of the feet, which clinically presents as thickened, scaly skin

Table. Reported Case of Psoriasis Alba

	Age/ Sex	Previous response to antifungals	Clinical appearance	Involved toes (interdigital space)	KOH and culture	Odor	Pathologic findings	Therapy/ Response to therapy
Case 1	Not stated	Refractory	Asymptomatic, white, sodden skin thickenings	Left 3rd, 4th Right 4th	-	-	Hyperkeratosis, atypical parakeratosis, acanthosis and an intact granular layer	Oral and ILI* of triamcinolon/ Rapid response was obtained but with the termination of therapy, relapse was common
Case 2	Not stated	Refractory	Asymptomatic, smooth white patch and an irregular white thickening	Right 3rd, 4th	-	-	Prominent vacuolization of the stratum corneum Hyperkeratosis, acanthosis and an intact granular layer	
Case 3	Not stated	Refractory	A painless erosive lesion with residual white islands	Left 3rd	-	-	Perinuclear vacuolation of cells of the stratum corneum with dot-like nuclear remnants Hyperkeratosis, acanthosis and a thinned granular layer	
Case 8	47/M	Refractory	Slightly itchy whitish, firm and pliant plaques	Left 4th Rright 4th	-	-	Confluent hyperkeratosis Absent stratum granulosum Subcorneal micropustule	Mometasone and calcitriol ointment/ successful treatment but tended to relapse after cessation of treatment
Our case 1	57/M	Refractory	Slightly pruritic white plaque	Left 3rd	-	-	Hyperkeratosis, atypical parakeratosis and a thinned granular layer	Pimecrolimus cream 1% / successful treatment with no side effects or signs of relapse
Our case 2	45/M	Refractory	Asymptomatic, white sodden plaques	Left 3rd Right 3rd	-	-	Hyperkeratosis, atypical parakeratosis, acanthosis and a thinned granular layer	

ILI*: intralesional injection

resembling a fungal infection but which shows negative KOH scrapings and is resistant to antifungal treatement. In 1961, Waisman[1] reported that a large proportion of such persistent interdigital dermatosis were in fact an atypical form of psoriasis, and termed the lesion psoriasis alba (interdigital psoriasis). Psoriasis alba occurs mostly between the toes and has an outstanding feature of a white sodden appearance, which is firm and pliant to the touch. With this sodden and macerated look, virtually every case of psoriasis alba is mistaken for an interdigital fungal infection and the patients have a long history of anti-fungal therapy with limited response. Both of our patients had been treated with antifungals for over 10 years before visiting the outpatient clinic. In many cases, there is concomitant involvement of other areas of the body when the patient presents with psoriasis alba[8]. Mommers et al.[8] suggested that when psoriatic stigmata was observed, psoriasis alba may be considered as an atypical form of intertriginous psoriasis. The patient in our first case had typical psoriatic plaques with adherent white silvery scales on both of his elbows and the buttocks, but our 2nd patient was clear from any psoriatic stigmata. Both had a negative family history of psoriasis. There is usually little or no itching in psoriasis alba[1,8] which was also observed in our patients. Psoriasis alba is known to appear in equal frequency in both sexes, but more severe manifestations have been reported in male patients[1]. The majority of patients are said to be in their 50s or 60s. A previous report[8] of psoriasis alba occurred in a 47-year-old man and our patients were 57 and 45 years old respectively, so the age range is similar. Unlike interdigital fungal infection, psoriasis alba sometimes occurs symmetrically and the fetid odor is usually absent[1], which was notable in our patients too.

Histopathological findings in interdigital psoriasis are in line with those found in the classical structure of psoriasis, but with variable alteration[1]. Hyperkeratosis and acanthosis are common and are usually accompanied by an atypical form of parakeratosis where perinuclear vacuolization of cells is commonly observed. But thinning of stratum granulosum[1] is rare and the Munro abscesses are sparse in psoriasis alba. From cases reported to date, only the one reported by Mommers[8] presented with a subcorneal micropustule. Although it is said that the spongiform pustules of Kogoj and Munro microabscesses are truly diagnostic of psoriasis[9], this may not be relevant in cases of psoriasis alba. In our patients, hyperkeratosis, atypical parakeratois, acanthosis and dermal inflammatory infiltrations through the rete were observed, along with a slightly thinned, granular layer. As stated above, the spongiform pustules of Munro and Kogoj were not found. A secondary fungal infection is possible in psoriasis alba but none of the reported cases including ours, stained positive with PAS[1,7].

The treatment of psoriasis alba is the same as for other forms of intertriginous psoriasis. Intertriginous psoriasis is difficult to treat due to side effects and recurrent relapses with traditional topical therapies[1,2,6]. At present, topical steroids are the mainstay in the treatment of interdigital psoriasis but are commonly associated with skin atrophy and the formation of striae, since penetration of the steroid is much easier in the areas where the skin is much thinner[6]. Calcipotriene, an alternative treatment for intertriginous psoriasis, is associated with local skin irritation, often requiring dilution[10,11]. Pimecrolimus cream 1% (Elidel®); Novartis Pharmaceuticals, East Hanover, NJ) is a nonsteroid, topical inflammatory cytokine inhibitor which is widely used in a number of inflammatory skin diseases[3]. The effectiveness of pimecrolimus cream 1% is comparable to that of clobestasol propionate 0.05% ointment[12] but in contrast with such mid to high potency topical steroids, pimecrolimus does not induce skin atrophy and has minimal side effects[13]. We initially prescribed a combination of clobetasol-17-propionate ointment (Dermovate®) and calcipotriol ointment (Diavonex®) to patient 1. Although improvement was observed, the patient complained of local skin irritation and subjective feelings of skin atrophy, which consequently led to lower compliance. Pimecrolimus cream 1% was tried as an alternative, and significant clearance of lesions was observed after 3 months. The cream did not cause any significant side effects and the patient did not suffer any relapse, which had been a major issue with terminating steroid. Pimecrolimus cream 1% was initially given to our second patient and an improvement was noted at the follow up visit after 1 month. So far, we have not noticed any side effects or signs of relapse.

In conclusion, the use of 1% pimecrolimus cream in our two cases demonstrates that topical application of pimecrolimus may be a safe and effective therapeutic option for psoriasis alba. Aside from the rapid clinical improvement, pimecrolimus cream 1%

was well tolerated in our patients, and no associated local irritation or skin atrophy was observed. In this paper, we present an overlooked clinical entity which has never been reported in Korea, and the appropriate treatment strategy.

REFERENCES

1. Waisman M: Interdigital psoriasis ("White Posriasis"). Arch Dermatol 1961;84:733-740.
2. Beerman H, Caro MR, Epstein NN, Farber EM, Montgomery N, Walsh AL: Abstract of discussion on interdigital psoriasis. Arch Dermatol 1961;84: 738-740.
3. Stuetz A, Grassberger M, Meingassner JG: Pimecrolimus (Elidel, SDZ ASM 981)- preclinical pharmacologic profile and skin selectivity. Semin Cutan Med Surg 2001;20:233-241.
4. Lebwohl MG, Heymann WR, Berth-Jones J, Coulson I: Treatment of skin disease: comprehensive therapeutic strategies. St Louis: Mosby; 2002.
5. Van de Kerkoff P: Papulosquamous and eczematous dermatoses: psoriasis. In: Bologna JL, Jorizzo JL, Rapini RP, editors. Dermatology. St Louis: Mosby; 2003. pp125-149.
6. Gribetz C, Ling M, Lebwohl M, Pariser D, et al.: Pimecrolimus cream 1% in the treatment of intertriginous psoriasis: a double-blind randomized study. J Am Acad Dermatol 2004;51:731-738.
7. Amichai B: Psoriasis of the glans penis in a child successfully treated with Elidel(r)(pimecrolimus) cream. J Eur Acad Dermatol Venereol 2004; 18: 742-3.
8. Mommers JM, Seyger MM, van der Vleuten CJ, van de Kerkhof PC: Interdigital psoriasis (psoriasis alba): Renewed attention for a neglected disorder. J Am Acad Dermatol 2004;51:317-318.
9. Mobini N, Toussaint S, Kamino H: Noninfectious erythematous papular and squamous diseases. In: Elder DE, Elenitsas R, Jonson BL Jr, et al.: Lever's Histopathology of the Skin, 9th ed. Philadelphia: Lippincott Williams & Wilkins; 2005, pp183-191.
10. Murdoch D, Clissold SP: Calcipotriol: A review of its pharmacological properties and therapeutic use in psoriasis vulgaris. Drugs 1992;43:415-429.
11. Kragballe K: Treatment of psoriasis with calcipotriol and other vitamin D analogues. J Am Acad Dermatol 1992;27:1001-1008.
12. Mrowietz U, Graeber M, Brautigam M, et al.: The novel ascomycin derivative SDZ ASM 981 is effective for psoriasis when used topically under occlusion. Br J Dermatol 1998;139:992-996.
13. Queille-Roussel C, Paul C, Duteil L, et al.: The new topical ascomycin derivative SDZ ASM 981 does not induce skin atrophy when applied to normal skin for 4 weeks: a randomized, double-blind controlled study. Br J Dermatol 2001;144: 507-513.