Granular Parakeratosis
-Report of Two Cases

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Granular parakeratosis (GP) is an uncommon, benign cutaneous eruption of intertriginous areas that represents a distinctive clinicopathologic entity. Clinically, GP presents with variably pruritic, hyperkeratotic, fissured papules and plaques over an erythematous base, affecting the cutaneous folds. Histological examination shows a characteristic picture with presence of abundant basophilic kerato-hyaline granules within a compact, hyperparakeratotic stratum corneum. We describe two cases of granular parakeratosis. In case one, the lesions cleared rapidly and completely after botulinum toxin injections to the axillae and groins. At 5-months’ follow-up, the patient remained asymptomatic. Case two is a 4-year-old boy with characteristic lesions in the groins associated with topical agents used. (Dermatol Sinica 25: 20-23, 2007)

Key words: Botulinum toxin, Granular parakeratosis, Hyperhidrosis

INTRODUCTION

In 1911 Northcutt et al. first reported five cases of axillary granular parakeratosis (GP).1-3 Granular parakeratosis presents as erythematous, red and/or brown keratotic or scaly papules or plaques that can be discrete, confluent, and/or reticulated, always affecting the intertriginous areas.4 GP can occur in patients of all ages and in both sexes although it seems more common in women.1 We herein reported two cases of granular parakeratosis and provided new treatment options.
CASE REPORT

Case 1. A 57-year-old man presented with a 3-year history of relapsing eruption. Initially it was in a discoid pattern but it became more widespread involving the axillae, antecubital fossae, groins and popliteal areas. Symptoms included itching and irritation. There was no reported history of change in skin care regimen or change in topical personal hygiene products, such as soap, or cleanser. The patient denied the application of antiperspirants, deodorants or perfume. The patient denied the presence of atopic diathesis or other previous skin abnormalities. His family history was unremarkable. The skin biopsy in Australia on 25 November 2003 showed pustular psoriasis and no fungus was found. This did not clinically correlate to his symptoms. He felt that the use of mometasone cream worsened his rashes and hence the medicine switched to betamethasone dipropionate ointment which was much helpful. This was followed by another bout of eruptions with secondary infection, which was settled after the use of topical potassium permanganate soaks as well as mupirocin calcium cream and methylprednisolone aceponate cream in Australia. He required a 1-month-course of acitretin in Hong Kong in 2004 with partial response first but without effect thereafter. Besides, he also had 4 courses of itraconazole under impression of tinea corporis in Hong Kong but without effect. He applied triamcinolone acetonide and econazole nitrate cream by himself in China since October 2005 with moderate response. Previous treatments included different topical emollients and cleansers. Due to persistent symptoms, he visited our clinic in November 2005. Physical examination revealed several hyperkeratotic, erythematous to brownish plaques with peripheral papular eruptions on the axillae, antecubital fossae, groins, perianal area and popliteal fossae. (Fig. 1A). Hyperhidrosis and maceration were found on the axillae and groins. A biopsy was performed on the edge of the lesion on the left axilla on his first clinic visit, and showed hyperparakeratosis and retained keratohyaline granules within the stratum corneum (Fig. 1B). He received intraleralal botulinum neurotoxin injections, commercially available as Botox® to the axillae (50U/axilla) and Dysport® to the groin areas (250U/groin area), with complete resolution of the rash within a few days. His antecubital fossae, perianal area and popliteal fossae were treated with topical 5% lactic acid (LactiCare lotion®(Stiefel) 5% lactic acid, 2.5% sodium pyrrolidone carboxylate). A follow-up examination 5 months later revealed no recurrence of the lesions (Fig. 1C and 1D). The axillae and groins remained dry.

Case 2. A 4-year-old boy developed well-defined, brownish, hyperkeratotic plaques on his groins for 1 month (Fig. 1E). The mother often washed the area thoroughly with water, followed by application of Esperson Ointment (Desoximetasone 0.25%) and Sinbaby Baby Lotion (each gram contains Zinc Oxide 100mg, Diphendrydamin 5mg, Dibucaine Hydrochloride 1.5mg, dl-Camphor 1.5mg, Benzalkonium Chloride 2.5mg, Silicone Oil 10mg). At the first clinical examination, the crusts were removed and sent for histopathologic examination, which revealed stratum corneum with thick, compact parakeratosis containing many cytoplasmic, basophilic granules with keratohyaline granules (Fig. 1F). The Sinbaby Baby Lotion and Esperson Ointment were discontinued. The lesions gradually resolved in a week.

DISCUSSION

Granular parakeratosis is characterized clinically by papules or well-defined erythematous and/or hyperpigmented hyperkeratotic plaques in the intertriginous areas.6 Clinical differential diagnosis included allergic contact dermatitis, irritant dermatitis, Hailey-Hailey disease, inverse psoriasis, tinea corporis, and intertrigo.

The etiology of GP remains obscure. In the normal maturation of keratinocytes from the stratum granulosum to the stratum corneum, histidine-rich profilaggrin precursors in the keratohyalin granules are broken down into many units of filaggrin in the cornified cells.7 These filaggrin aggregates serve as an adhesive matrix for the keratin filaments during the process of
cornification. However, in patients with granular parakeratosis, the process of complete breakdown of the filaggrin precursor units does not appear to occur. GP may be a non-specific pathologic process to different topical irritants. It has been speculated that an antiperspirant or deodorant was altering the normal maturation of keratinocytes and causing corneocytes to retain keratohyaline granules abnormally. Mehregan et al. also state that this eruption, found in only moist intertriginous areas, could be due to mechanical irritation that induces secondary changes in the skin. Water and sweat are known irritants to the skin. The combinations of heat, moisture and friction in the cutaneous folds are contributory factors in compromising the barrier function of the epidermis, thus enabling penetration of irritants into the skin. It remains possible, however, that GP represents an unusual reaction to an unrecognized ingredient or component of another type of skin care product. Because most of the eruptions in case 1 involved skin fold, it is likely that occlusion and retention of moisture are at least indirectly involved in the development of the disorder. Nevertheless, the role of topical steroids or skin care products cannot be excluded.

The characteristic histologic hallmark of GP consisted of severe compact parakeratosis, with retention of keratohyalin granules throughout the stratum corneum, and vascular proliferation and ectasia. Generally, the parakeratotic stratum corneum is markedly thickened, and the epidermis itself tends to be acanthotic. The stratum granulosum is usually intact, and of normal or slightly increased thickness. In case 1, there was partial parakeratosis in the cornified layer with slight compact hyperkeratosis, perhaps because the biopsy specimen was taken from the edge of the lesion. A skin biopsy was not performed in case 2 because of young age. The diagnosis of GP was based on the characteristic clinical features and pathological examination of the easily removed crusts, since the distinct GP histopathologic features are only seen in the cornified layer.

In 2002, Trowers et al. reported the first infant with GP. At present, there are a total of 12 children documented with GP in the diaper region including the case 2 in this report. The ages at presentation of the children reported ranged from 9 months to 6 years old. Almost all children were using topical application containing zinc oxide or wearing diaper. Case 2 in this report was 4 years old and did not wear diaper for a long time. But he had been treated with Sinbaby Baby Lotion and Esperson Ointment. Jin et al. showed that zinc oxide applied topically to both incised and intact mouse skin significantly increased the mitotic index of the epidermal basal cells. The hyperkeratotic and acanthotic appearance of GP may be due in part to these same effects of topical zinc oxide on human skin. Granular parakeratosis is likely an

**Fig. 1**
(A) Case 1. Well-defined, brownish, hyperkeratotic plaques on the popliteal fossae. (B) Case 1. There was only partial parakeratosis in the cornified layer with slight compact hyperkeratosis. (C) Case 1. Erythematous, hyperkeratotic plaques on the right axilla and upper arm. (D) Case 1. A follow-up examination 5 months later revealed no recurrence of the lesions. (E) Case 2. There are well-demarcated, erythematous plaques with thick desquamating hyperkeratotic scale along the inguinal areas. (F) Case 2. Compact parakeratosis composed of cells with many cytoplasmic granules with keratohyalin characteristics. (Hematoxylin and cosin, x 400)
under reported reaction that should be considered in the differential diagnosis when children present with a hyperkeratotic dermatitis, particularly in the diaper area, where zinc oxide is often applied for various dermatoses.

The management of GP have variable efficacy. In the literature, most eruptions cleared after discontinuation of the topical product (deodorants, creams, perfumes, etc.) as in case 2. Clearance may be occurred in case 1 if he stops using topical products and decreases hydration and maceration of the skin. The topical and systemic administration of steroids, retinoids, immunomodulators, antibiotics, and antifungal agents were of variable efficacy. Topical steroid had been shown to cause skin atrophy and epidermal barrier disturbance. Lactic acid is an effective keratolytic and has been used in the reversal of epidermal atrophy from topical steroid. It is possible that the excessive cellular cohesion that results from abnormal keratinocyte differentiation can be effectively relieved by keratolytics, such as lactic acid. The case 1 applied lactic acid to the antecubital fossae and popliteal areas once a day and the lesions cleared completely. Spontaneous remission also occurred in some cases.

There have been two reported cases of patients with GP who also suffered from hyperhidrosis. The relationship between hyperhidrosis and GP is elusive, although sweat is a well-known irritant. Botulinum toxin is an effective treatment of axillary hyperhidrosis. The efficacy of Clostridium botulinum type A neurotoxin in the treatment of hyperhidrosis lies in its ability to interrupt sympathetic stimulation of eccrine sweat glands. This pharmacologic denervation produces a lasting and yet reversible marked decrease in or complete absence of sweating. However, because of the possible irritancy of lactic acid on axillae and groins, botulinum toxin is used for the treatment. Our first case responded rapidly to treatment, and remained in remission at 5-months’ follow-up. Botulinum toxin injection therapy may provide rapid and long-term remission in cases of GP who also suffered from hyperhidrosis.

REFERENCES