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Case Report

Two men with papular acantholytic dyskeratosis of the genitocrural area (PADGA) in Hong Kong

香港兩名患有生殖腹股區域的丘疹性棘層鬆解性角化不良的男仕

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Papular acantholytic dyskeratosis (PADGA) of the genitocrural area is rare. The aetiology, clinical and histological appearances overlap with Darier's disease and Hailey-Hailey disease. As they may be initially misdiagnosed as sexually transmitted infections, skin biopsy is necessary for diagnosis. In this article, we illustrate two men with PADGA, from the clinical course, diagnosis, to treatment.

生殖腹股區域的丘疹性棘層鬆解性角化不良是罕見病。其病因學、臨床和組織學表現與達里埃氏病和家族性良性慢性天疱瘡相重疊。此病初診時常被誤診為性病，需進行皮膚活檢以確立診斷。在本文中，我們通過臨床過程、診斷到治療部份闡述生殖腹股區域的丘疹性棘層鬆解性角化不良的兩宗男仕病例。

Keywords: Acantholysis, Male, Perineum

關鍵詞：棘層松解、男性、會陰

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Introduction

Papular acantholytic dyskeratosis of the genitocrural area (PADGA) was first reported in 1977 in a female.[1] Since then, many cases have been reported and predominantly in females. No cases have been reported in Hong Kong so far. Herein, we report two cases of PADGA and to the best of our knowledge, these are the first reported cases of this entity in Hong Kong.

Case report

Patient 1

A 54-year-old man with good past health presented with a three-year history of a mildly itchy rash over his perianal area. He had no bowel symptoms, and was a social alcoholic drinker and smoker. On examination, an erythematous erosive indurated plaque was noted in the perianal area extending to gluteal cleft (Figure 1). The differential diagnoses included perianal streptococcal dermatitis, condyloma acuminata or lata, squamous cell carcinoma, extramammary Paget's disease, Hailey-Hailey disease and pemphigus vegetans.

A skin biopsy was performed which showed hyperkeratosis, parakeratosis and acanthosis in the epidermis together with mild superficial perivascular lymphocytic infiltration. There were mild acantholytic changes with various degrees of dehiscence of the keratinocytes (Figure 2a). In addition, there were relatively broad zones of dyskeratosis as evidenced by the presence of brightly eosinophilic cytoplasm, corps ronds and grains (Figure 2b). He was treated topical steroids with poor response. He defaulted subsequent follow-up.

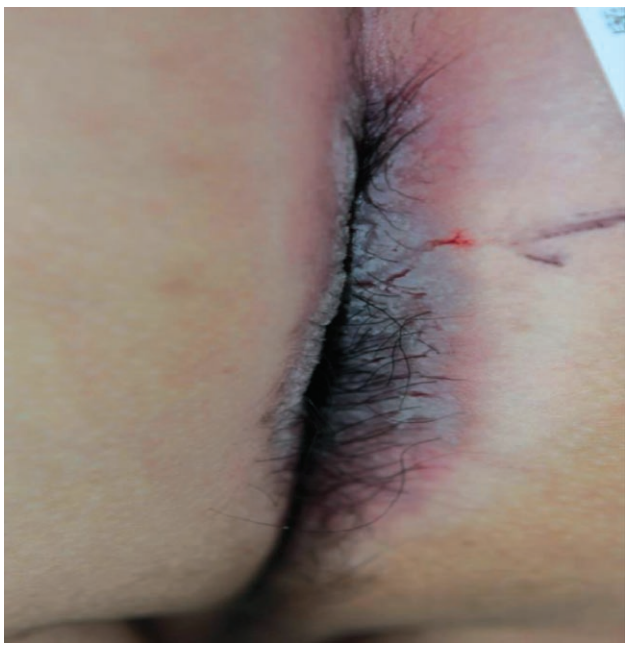

Figure 1. Macerated eroded erythematous plaque over gluteal cleft of Patient 1.

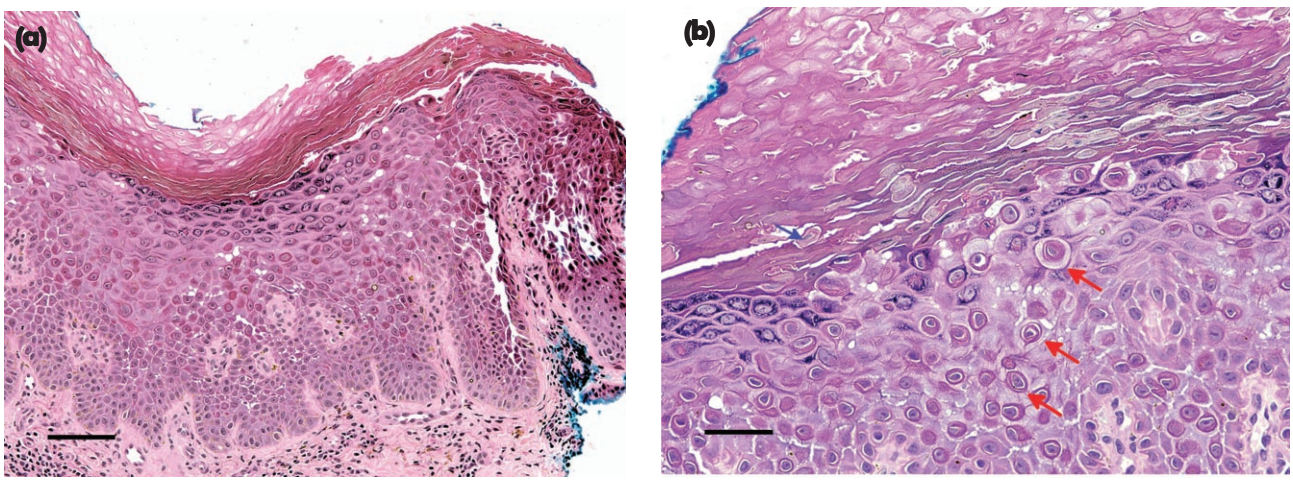

Figure 2. (a) Hyperkeratosis, parakeratosis, acanthosis and with mild acantholytic change. The acantholytic change is more prominent in the right field. (H&E stain, marker 80 micron). (b) Broad zone of dyskeratosis with corps ronds (red arrows) and grains (blue arrow). (H&E stain, marker 40 micron).

Patient 2

A 67-year-old man presented with a few months history of asymptomatic papules in the left groin. He did not have other skin or nail abnormality. There was no family history of skin disease and no sexual activity for more than 10 years. For his past health, he had type 2 diabetes mellitus, hypertension, end-stage renal failure, and history of diclofenac-induced Stevens Johnson syndrome.

On examination, monomorphic eroded white papules were seen on his left groin (Figure 3). The right groin and perianal area were not involved. Differential diagnosis included segmental Darier's disease, Hailey-Hailey disease, epidermal naevus, seborrheic keratoses, genital warts, and herpes genitalis. He declined blood testing for HIV, syphilis, and lesion swab for herpes simplex. Gross examination of the skin biopsy revealed papules of around 4 mm in size. On histological examination, there were several foci of acantholytic dyskeratosis. Hyperkeratosis, parakeratosis, intraepidermal acantholysis (Figure 4a) and tiers of dyskeratosis and corp ronds (Figure 4b) were present. Although 1% hydrocortisone cream was given, compliance was poor as the condition was asymptomatic.

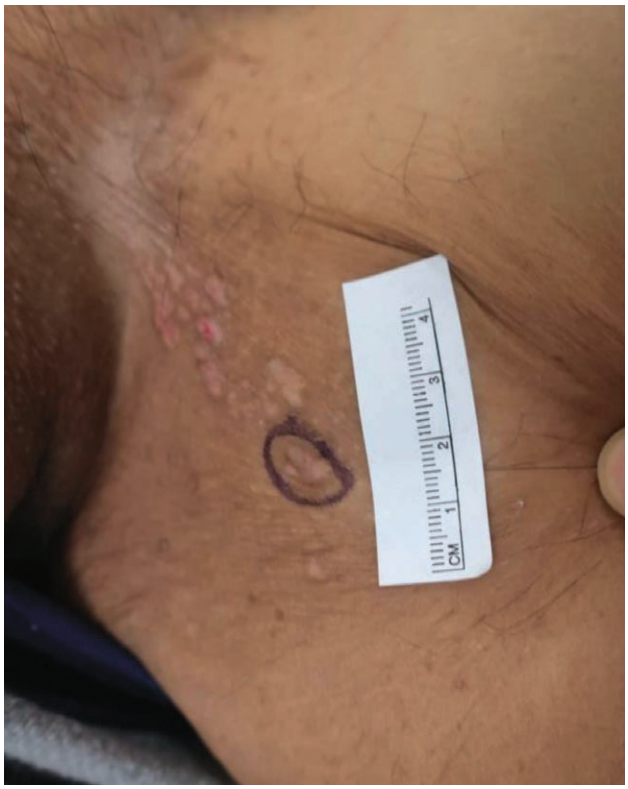

Figure 3. Monomorphic eroded white papules over left groin of Patient 2.

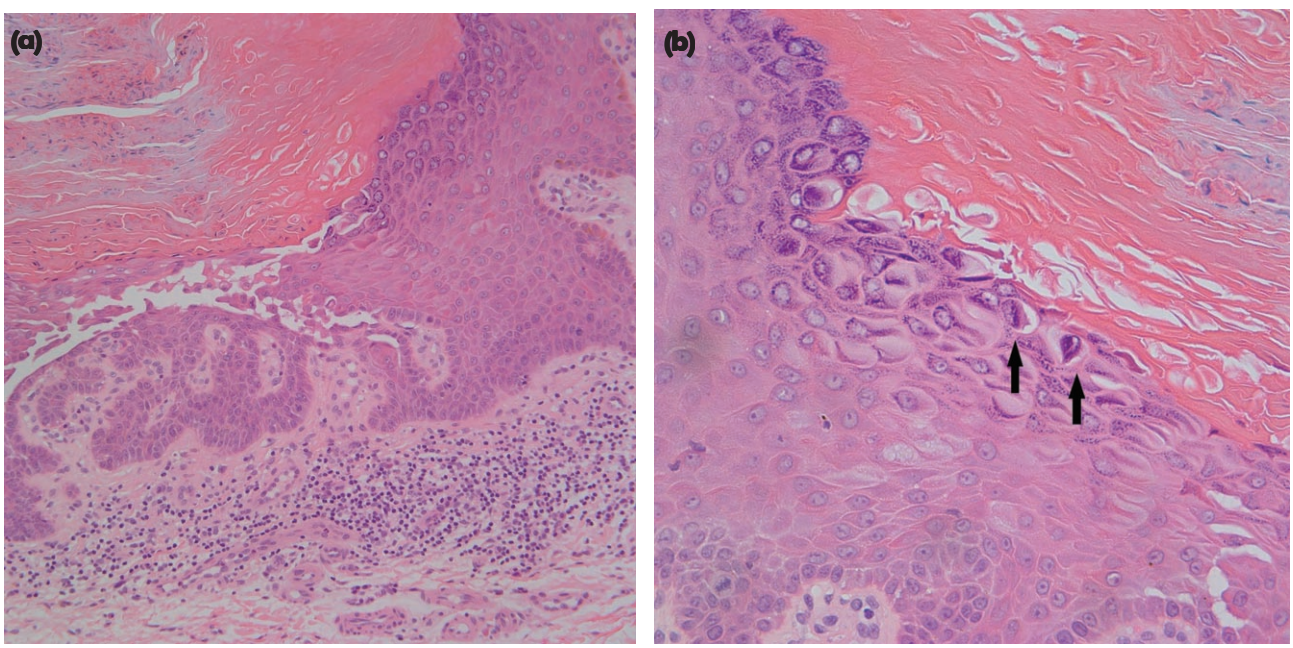

Figure 4. (a) Intraepidermal acantholysis with tiers of dyskeratosis. H&E, magnification x200. (b) Corps ronds (arrows) as shown. H&E, magnification x400.

Discussion

PADGA is a recently described entity, not often found in dermatology textbooks. There have been less than 20 reports in male patients with PADGA in the literature so far, some of which are listed in Table 1.

The aetiology of PADGA is not well understood, although somatic mosaicism of ATP2A2, ATP2C1 mutations in the lesional skin may be responsible.[6,7] The diagnosis is not often suspected initially but should always be borne in mind. Patients may complain of some white coloured papules in the genitalia, groin, or perianal area which may be

Table 1. Clinical and histopathological features of reported male cases

Study	Case	Sex	Age	Sites	Clinical appearance	Histology / Genetic testing	Outcomes
Frances et al, 1984[2]	1	M	–	Genitalia		Epithelial hyperplasia, dyskeratosis	Responded: Etretinate, topical 5-fluorouracil
	2	M	–	Genitalia			Failed: surgical excision
Verma, 2013[3]	3	M	26	Perianal/ perineal	Grayish white confluent papules with eroded areas	Hyperkeratosis, acantholytic dyskeratosis, suprabasal cleft formation	Responded: 0.1% tacrolimus ointment Failed: potent topical steroid, oral antihistamines.
Al-Muriesh et al, 2016[4]	4	M	9	Perianal	White plaque	Hyperkeratosis, suprabasal acantholysis, dyskeratosis	
	5	M	34	Perianal, perineum	Small grayish, skin-colored papules and plaques	Hyperkeratosis, acantholysis, epidermal clefting, dyskeratotic cells	
	6	M	52	Scrotum, inner thigh	Whitish plaques with crusts and erosions		Symptomatic response but lesions persisted: mometasone furoate cream, zinc oxide paste, oral desloratadine 8.8 mg qd
	7	M	47	Perineal, scrotal and inner thigh areas	Dark-brown, skin-coluored papules and plaque	Hyperkeratosis and parakeratosis, acanthosis with a suprabasal cleft, acantholytic and dyskeratosis	Symptomatic response but lesions persisted: oral antihistamine and topical mometasone furoate cream
Lee et al, 2017[5]	8	M	49	Bilateral inguinal areas	Pruritic papular eruption	Hyperkeratosis, acanthosis, suprabasal cleft with villi, numerous typical acantholytic dyskeratotic cells in the stratum corneum and spinosum.	Failed response: 0.1% topical mometasone furoate, systemic steroid, acitretin

macerated. Clinically, they may be initially misdiagnosed as sexually transmitted infections (i.e. genital wart, molluscum contagiosum, herpes genitalium etc) or other skin diseases such as epidermal naevus, seborrheic keratosis, Darier's disease or Hailey-Hailey disease. The final diagnosis is based on clinical and histopathological findings. Despite the characteristic appearance of a mixed Darier and Hailey-Hailey like pattern,[8] the role of skin biopsy is primarily to confirm presence of acantholytic dyskeratosis. From the literature and in our patients, the acantholytic dyskeratotic changes is extensive, affecting a significant portion of the specimen. Hence, if only small foci are found, these are likely to be incidental findings of focal acantholytic dyskeratosis and one should consider other entities such as epidermal naevus, particularly in the paediatric population. Therefore, a good size biopsy is also important to facilitate the interpretation. Segmental or limited forms of Darier disease and Hailey-Hailey disease should also be clinically excluded by looking for personal or family history of typical lesions elsewhere and ascertaining that the lesion does not follow Blaschko's lines.

Currently, treatment is not well-established for PADGA. For asymptomatic patients, observation is all that is necessary. For symptomatic cases, treatments include topical corticosteroids,[4] topical tacrolimus,[9] and vitamin D analogues;[10] while systemic retinoids,[1] and cyclosporin[11] can be tried in patients with severe or refractory disease. Furthermore, non-pharmacological treatments such as ablative laser therapy may also be considered.[12]

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