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CASE REPORT

Papular Acantholytic Dyskeratosis of the Vulva: A Case Report and Literature Review

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Abstract: Papular acantholytic dyskeratosis (PAD) of the vulva is an uncommon benign condition characterized by multiple hyperkeratotic papules in the anogenital region. First described in 1984, PAD belongs to the spectrum of focal acantholytic dyskeratoses and shares histopathological features with Darier disease and Hailey-Hailey disease. Despite its persistence, PAD is benign, requiring only reassurance in many cases. However, various treatment modalities have been reported for symptomatic patients, including topical and systemic therapies, and procedural interventions. We present a case of a 21-year-old Thai woman with asymptomatic perivulvar papules with typical histopathological features of PAD. After conservative management, the patient remained asymptomatic during follow-up. Additionally, we present a review of the current literature on this uncommon entity. This case highlights the importance of clinicopathological correlation in diagnosing PAD and distinguishing it from other clinically similar disorders. We discuss the clinical presentation, histopathological features, differential diagnosis, potential genetic associations, and management options for PAD.

Keywords: benign tumor, Darier disease, focal acantholytic dyskeratosis, genetic, genital papule, Hailey-Hailey disease

Introduction

Papular acantholytic dyskeratosis (PAD) of the vulva is a rare dermatological condition characterized by the development of multiple, small, hyperkeratotic papules on the perivulvar area and inner thighs.[1] It is often misdiagnosed due to its rarity and similarity to other vulvar lesions. The condition is categorized under the spectrum of focal acantholytic dyskeratoses, a distinctive histopathological pattern of suprabasal clefts, acantholytic and dyskeratotic cells, and hyperkeratosis and parakeratosis, first conceptualized by Ackerman in 1972.[2] PAD has been known by various names, including genitoperineal papular acantholytic dyskeratosis, papular acantholytic dyskeratosis of the anogenital/genito-crural area, and papular acantholytic dermatosis.[3,4] This terminology reflects the evolving understanding of the condition and its anatomical distribution.

In 1984, Chorzelski et al first coined the term "papular acantholytic dyskeratosis", describing a 23-year-old woman with multiple, persistent papules on the vulva, establishing PAD as a distinct dermatological entity.[5] Throughout the 1990s and early 2000s, dermatologists and gynecologists gradually became more aware of PAD, leading to an increase in reported cases and a better understanding of its clinical spectrum.[6–9] Recent studies have suggested potential genetic links to other acantholytic disorders, broadening the clinical spectrum of PAD. Here, we present a case of PAD in a 21-year-old Thai woman, contributing to the growing body of literature on this rare condition.

Case Presentation

A 21-year-old Thai woman presented to our dermatology clinic with a two-month history of multiple asymptomatic papules on the perivulvar area and inner thighs. The patient reported a gradual increase in the number of lesions over time, denying any previous treatment, trauma, or family history of similar manifestations. Her past medical history was significant for well-controlled Graves' disease, managed with oral methimazole. Physical examination revealed multiple

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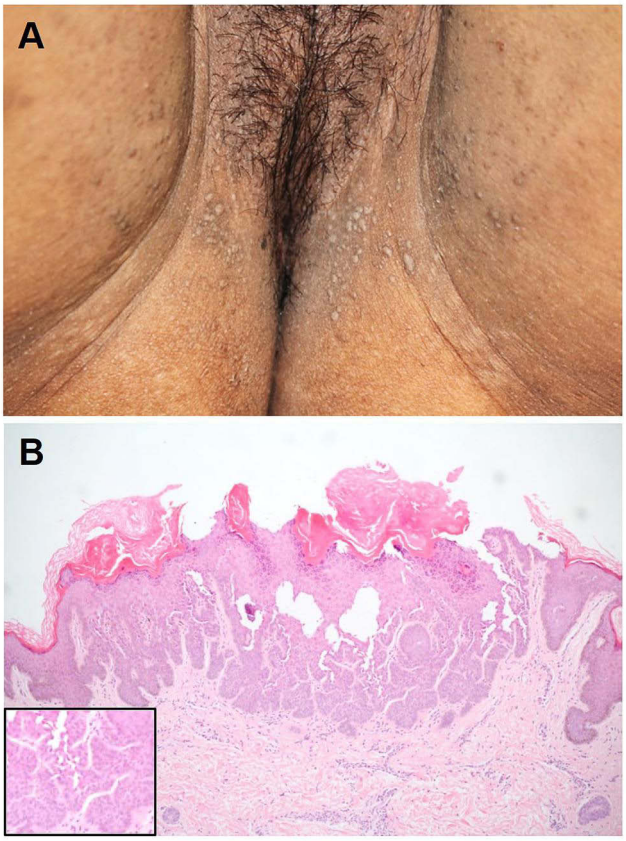

Figure 1 Clinical manifestations **(A)**: multiple hyperkeratotic, skin-colored, flat-topped papules localized to the perivulvar region and bilateral inner thighs; Histopathological findings **(B)**: hyperkeratosis, hypergranulosis, and papillomatous epidermal hyperplasia with focal acantholytic dyskeratosis in the epidermis (hematoxylin-eosin, original magnification x40; inset demonstrating high-power view).

hyperkeratotic, skin-colored, flat-topped papules localized to the perivulvar region and bilateral inner thighs (Figure 1A). No other cutaneous, mucosal, or nail abnormalities were observed, and examinations of other organ systems were unremarkable.

The differential diagnosis at this stage encompassed several entities, including flat warts, eruptive syringoma, lichen nitidus, lichen planus, and inverted follicular keratosis. However, the distribution pattern and morphology of the lesions were inconsistent with typical presentations of eruptive syringoma or lichen nitidus, while the lack of violaceous hue or Wickham's striae argued against lichen planus. To establish a definitive diagnosis, a punch biopsy was performed on a lesion from the left thigh. Histopathological analysis demonstrated hyperkeratosis, hypergranulosis, and papillomatous epidermal hyperplasia with focal acantholytic dyskeratosis in the epidermis (Figure 1B). These findings, in conjunction with the clinical presentation, led to the diagnosis of PAD.

Given the benign nature of the condition and the patient's lack of symptoms, a conservative management approach was adopted after discussion with the patient. The patient was provided with a comprehensive explanation of the diagnosis, emphasizing its benign course and non-malignant nature. No specific therapeutic intervention was initiated, aligning with the current standard of care for asymptomatic cases. The patient agreed to regular follow-up appointments for monitoring. The patient remained asymptomatic during her follow-up visits over six months, with no significant progression of the lesions.

Discussion

PAD is a rare, benign dermatological condition with limited epidemiological data available. Its prevalence is difficult to determine precisely due to its rarity and potential underdiagnosis. Since its first description in 1984, fewer than 50 cases

Table 1 Previously Reported Cases of Early-Onset Papular Acantholytic Dyskeratosis of the Vulva

No.	Author(s)	Year	Age	Age of Onset	Clinical Features	Treatment	Outcome
1	Chorzelski et al[5]	1984	23	6 years	Grouped papules on labia majora, some with ulceration	Electrocauterization	Some papules were completely removed.
2	Cooper[11]	1989	28	Several years	Multiple isolated white papules on the labia majora	0.05% topical tretinoin cream	Responded temporarily but persistent after 12 months
3	Sáenz et al[12]	2005	11	6 months	Scattered, skin-colored, and whitish keratotic papules, and multiple grouped superficial erosions on the labia majora	No treatment	Spontaneously improved lesions at three years follow-up
4	Wang et al[13]	2009	8	8 months	Scattered, skin-colored, whitish papules located on the inner aspect of the labia majora of the vulva	3% boric acid solution	Decreased number of lesions after three months
5	Yu et al[14]	2016	20	10 years	Discrete hyperkeratotic papules over the perianal skin and the labia majora with family history of Hailey-Hailey disease	Not specified	Follow-up not detailed
6	Harrell et al[15]	2020	30	9 years	Agminated papules forming plaques on the labia majora and multiple skin-colored papules on the inner thighs and perianal skin	Not specified	Follow-up not detailed

have been reported in the literature.[1] The condition has no ethnic preference and appears to have a predilection for females, with only a few cases reported in males.[3,4,10] Our patient presented an unusual age of onset of PAD; her age of 21 years was atypical, as PAD most commonly affects women in their fourth to fifth decades of life.[1] Table 1 summarizes the key features of previously reported early-onset PAD cases in the literature, including patient demographics, clinical presentation, treatment approaches, and outcomes.[5,11–15]

The diagnosis of PAD requires both clinical and histopathological correlation. Clinical manifestation of PAD typically reveals multiple discrete, skin-colored to white, flat-topped papules ranging from 2–5 mm in diameter. The lesions are usually symmetrically distributed on the vulva and perineum and sometimes extend to the inner thighs or perianal area.[1,12,16,17] In our case, the patient presented with characteristic multiple small hyperkeratotic, skin-colored papules on the perivulvar area and inner thighs, consistent with typical PAD presentation. However, the asymptomatic nature of her lesions was uncommon, as two-thirds of reported cases describe pruritus or burning sensation.[1]

Histopathological features of PAD demonstrate a distinctive pattern of acantholysis and dyskeratosis. Key features include suprabasal clefting, acantholysis, and dyskeratosis characterized by deeply eosinophilic cytoplasm and pyknotic nuclei. Corps ronds and grains are typically seen in the upper layers of the epidermis. The stratum corneum often shows hyperkeratosis and parakeratosis.[18] However, PAD shares histopathological features with both Hailey-Hailey disease and Darier disease, as all three conditions display acantholysis and dyskeratosis. Key clinical and histopathological differences that distinguish PAD from these two inherited acantholytic disorders are summarized in Table 2. In our case, skin biopsy effectively excluded the initially considered differential diagnoses, ie, flat warts, eruptive syringoma, lichen nitidus, and lichen planus, as they lacked the characteristic acantholytic dyskeratosis observed in this condition.

Table 2 Clinical and Histopathological Differences Among Popular Acantholytic Dyskeratosis, Hailey-Hailey Disease, and Darier Disease

Condition	Clinical Features	Histopathological Features
Papular acantholytic dyskeratosis	Small, hyperkeratotic papules in the anogenital area, typically asymptomatic or mildly pruritic	Suprabasal acantholysis, dyskeratosis, corps ronds and grains, papillomatous hyperplasia, hyperkeratosis, parakeratosis
Hailey-Hailey disease	Painful recurrent vesicles and erosions in intertriginous areas (eg, axilla, groin), exacerbated by heat and friction	Extensive acantholysis (dilapidated brick wall appearance), minimal dyskeratosis, often associated with secondary infection
Darier disease	Greasy hyperkeratotic papules in seborrheic areas (eg, scalp, chest, back), nail abnormalities, pruritus	Suprabasal acantholysis, dyskeratosis, hyperkeratosis, corps ronds and grains, papillomatosis

The etiology of PAD remains unclear. While most cases appear to be sporadic, recent genetic studies have identified mutations in some patients, suggesting potential links to other acantholytic disorders. In 2012, Pernet et al reported a familial case with an ATP2C1 mutation, proposing an allelic relationship to Hailey-Hailey disease.[19] Subsequently, in 2015, Knopp et al described a case with an ATP2A2 mutation, suggesting PAD could represent somatic mosaicism of Darier disease in some instances.[20] Additionally, a rare case of acantholytic dyskeratosis presenting with clinical features of vulval lichen sclerosus has been reported, further complicating the clinical picture of these disorders.[21]

Management of PAD remains challenging, and no standardized treatment protocol exists due to its rarity and the lack of large-scale studies. The management of asymptomatic PAD patients remains controversial. Although benign, there is no consensus on the need for long-term monitoring or biopsies, particularly given the unpredictable nature of the disease progression. Symptomatic patients have been reported with variable treatment success, topical and systemic corticosteroids are often used as first-line therapy.[22,23] Topical and oral retinoids have shown efficacy in some cases.[11,13,15,24] Procedural interventions such as excision, ablative laser therapy, and cryotherapy have also been employed.[25,26] Interestingly, the spontaneous resolution has been reported in two cases, highlighting the unpredictable nature of this condition.[12,27]

A novel treatment approach using topical diclofenac sodium 3% gel has shown promising results in a recent case report.[28] This treatment was well-tolerated and led to complete remission of lesions after two months of application, with no relapse reported over a two-year follow-up period. This offers a potential new therapeutic option for PAD that warrants further investigation. Genetic studies linking PAD to mutations in ATP2C1 and ATP2A2 highlight the need for further research to clarify PAD's place in the spectrum of acantholytic dyskeratoses. Given the potential genetic associations, genetic testing and counseling may sometimes be considered. Establishing a long-term follow-up plan is crucial to monitor for any changes in the lesions or development of symptoms over time.

Conclusion

This case of PAD in a young, asymptomatic Thai woman underscores the importance of considering PAD in the differential diagnosis of anogenital papular lesions across all age groups. It highlights the crucial role of histopathological examination in confirming the diagnosis and differentiating PAD from other clinically similar conditions. While often persistent, PAD is benign, and management should be tailored to the patient's symptoms and preferences. Further studies are needed to elucidate the pathogenesis of PAD, investigate its genetic basis, establish evidence-based treatment guidelines, and explore the long-term prognosis of this rare but intriguing dermatological condition.

Ethics Approval and Consent to Participate

This article was performed in accordance with the principles of Declaration of Helsinki. Ethical review and approval was not required to publish the case details in accordance with the local legislation and institutional requirements. Written informed consent was obtained from the patient for publication of this case report and any accompanying images as per our standard institutional rules.

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