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Case Report **OPEN ACCESS**

Darier's disease masquerading as eczema: A case report and diagnostic challenges

Asilah Abd Rahim [1], Rosediani Muhamad [1]*, Azlina Ishak [1], Norazlima Mohd Ali [2]

[1] Department of Family Medicine, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, Kelantan, MALAYSIA
[2] Department of Dermatology, Hospital Pulau Pinang, Health, George Town, Pulau Pinang, MALAYSIA
***Corresponding Author:** rosesyam@usm.my**

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ABSTRACT

Darier's disease (DD) is a rare autosomal dominant genodermatosis that is commonly presented by hyperkeratotic papules and some may have nail dystrophy changes. However, due to its clinical featured resemble common dermatological conditions such as eczema or seborrheic dermatitis, leading to misdiagnosis and prolonged ineffective treatment. We presented a case of 47-year-old man with a history of long-standing pruritic papules affecting the face, neck, upper chest, anterior torso, and lower abdomen include distal nail splitting changes. His first symptoms appear during adolescence, progressively worsened over time and were aggravated by sun exposure, heat, as well as seafood consumption. Despite numerous medical consultations and treatment with topical corticosteroids as well emollients, his condition remained unchanged. A positive family history of similar skin manifestations prompted further evaluation. A skin biopsy was done and confirmed DD based on hallmark histopathological findings, including suprabasal acantholysis, corps ronds, and dyskeratosis. He then started on acitretin 35 mg daily and topical emollients. With a proper targeted treatment his symptoms response well based on eight weeks follow up. This case highlights the diagnostic challenges of DD in primary care and underscores the importance of recognizing its distinctive clinical and histopathological features. Early diagnosis and appropriate management with systemic retinoids and supportive therapy can significantly improve patient outcomes and quality of life.

Keywords: eczema, Darier's disease

INTRODUCTION

Darier's disease (DD) is a rare autosomal dominant genodermatosis caused by mutations in the ATP2A2 gene, leading to defective keratinocyte adhesion and impaired epidermal integrity [1, 2]. It is typically presents in adolescence with chronic, pruritic, hyperkeratotic papules affecting seborrheic areas such as the face, neck, upper chest, and back. They may present nail abnormalities such as distal splitting and longitudinal streaks, which are hallmark key features [3]. The disease is usually exacerbated by heat, humidity, ultraviolet exposure, and mechanical irritation. Despite an unnecessary active clinical features, DD is frequently misdiagnosed as eczema, seborrheic dermatitis, or fungal infections which may resulting in prolonged ineffective treatment and create unnecessary burden to patient. A definitive diagnosis requires histopathological confirmation [1, 4]. Here, we report a case that highlights the challenges of diagnosing DD in primary care settings and emphasizing the need for clinical suspicion in patients with persistent skin lesions unresponsive to conventional treatments. By recognizing DD early, besides initiating appropriate management, clinicians can prevent unnecessary delays in treatment, improve symptom control, and enhance patient quality of life.

CASE REPORT

A 47-year-old gentleman presented with a history of longstanding distal nail splitting and multiple pruritic rashes and papules over the face, neck, upper chest, anterior torso and lower abdomen. The lesions first appeared during his teenage years and progressively worsened over time. The pruritus was exacerbated by exposure to sunlight, warm weather, heat, and seafood intake.

He initially sought medical treatment at private clinics then primary care centers and diagnosed himself with eczema. Eczema treatment include topical corticosteroids, and aqueous cream was prescribed for him. However, despite adherence to treatment for years, his symptoms persisted without improvement. He was referred to a dermatology clinic for further evaluation and a detailed history revealed a positive family history of similar skin manifestations, as both his mother and grandmother had experienced the same symptoms and skin changes as him.

On physical examination, multiple skin-colored to brownish hyperkeratotic papules coalescing into plaques over the face, neck, upper chest, anterior torso, and lower abdomen (**Figure 1** and **Figure 2**).

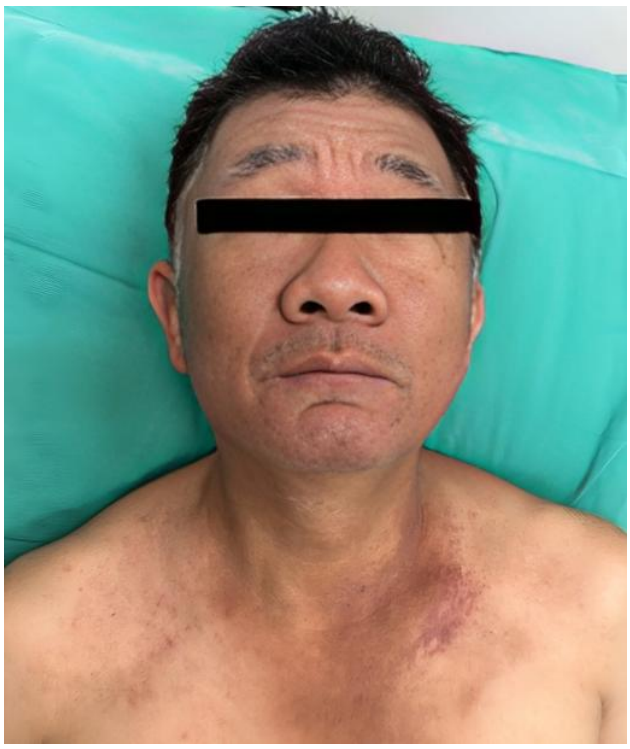

Figure 1. Multiple skin-colored hyperkeratotic papules coalescing into plagues on the face, neck leading to early leonine facies (Reprinted with permission of the patient)

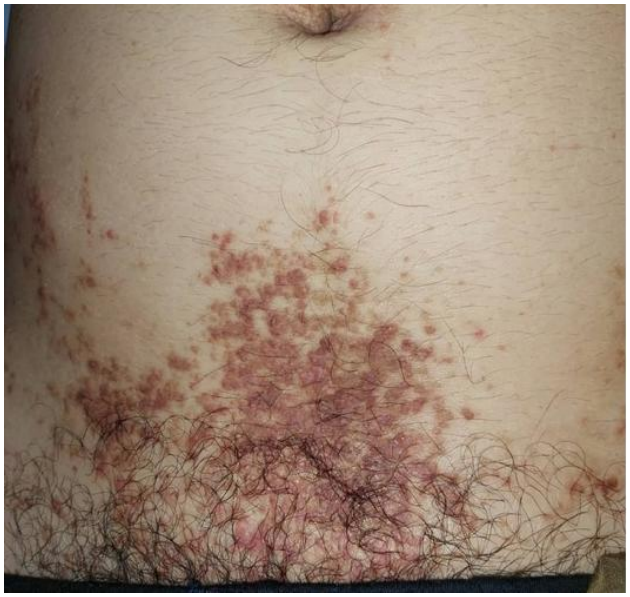

Figure 2. Multiple hyperpigmented brownish, verrucous papules and form plaques over the lower part of abdomen (Reprinted with permission of the patient)

Examination of the nails revealed distal splitting (**Figure 3**), while the palms and soles exhibited thickened skin. The scalp and oral mucosa were unremarkable, with no visible lesions.

A skin biopsy was performed, and histopathological examination revealed hallmark features consistent with DD which are present of suprabasal acantholysis and clefting with retention of the basal keratinocyte layer. Dyskeratotic cells, including corps ronds and grains, were observed, along with hyperkeratosis, parakeratosis, and hyper-granulosis. Mild perivascular lymphocytic infiltration was present, to suggest

Figure 3. Longitudinal ridges seen with a V-shaped nick at the free edge of the nails (Reprinted with permission of the patient)

no evidence of malignancy or fungal infection. These findings were consistent and confirmed the diagnosis of DD.

Following the diagnosis, the patient was started on acitretin 35 mg daily, loratadine 10 mg daily, and topical therapy with 10% urea cream applied twice daily, along with 40% liquid paraffin mixed with 60% white soft paraffin to apply three times daily. He also counseled on avoidance of excessive heat exposure, avoid excessive sun exposure and proper skin hygiene.

At an eight-week follow-up visit, he demonstrated significant clinical improvement. His condition remained stable, and he reported better symptom control with the prescribed regimen.

DISCUSSION

DD is a rare genetic skin disorder that is rarely encountered in primary care, making it prone to misdiagnosis and subsequently lead to under treatment. It is a hereditary condition caused by mutations in the ATP2A2 gene, DD disrupts keratinocyte adhesion, leading to chronic and relapsing skin lesions [1, 5]. DD typically presented with pruritic, hyperkeratotic papules that predominantly affecting seborrheic regions such as the face, neck, upper chest, and back [6, 7]. Nail abnormalities such as distal splitting and longitudinal streaks are clinical key features for DD [2, 3]. However, due to its clinical features that are similar to more common dermatological conditions such as eczema, seborrheic dermatitis and fungal infections, DD is often misdiagnosed in primary care settings [8, 9]. This case illustrates the significant role of primary care physicians (PCPs) in the early identification of DD, the challenges in its diagnosis, and the importance of appropriate referral and management.

The overlapping features of DD with other common skin condition in primary care cause diagnostic challenge at primary care level. Patients with DD frequently present with pruritic, scaly eruptions that resemble eczematous dermatitis and as a consequences lead to empirical treatment with topical corticosteroids and emollients [4, 10]. While these may provide short term symptomatic relief but their ineffectiveness in long-term symptom control should prompt reconsideration of the other diagnosis. In this case, the patient underwent several years of unsuccessful treatment for presumed eczema before referral to dermatology for a proper diagnosis. Other factor contributing to diagnostic difficulty is the unrecognized nail abnormalities, which are a hallmark of DD [2, 3]. Nail features such as longitudinal streaks, distal splitting and subungual

hyperkeratosis often go unnoticed or are misattributed to as onychomycosis. A thorough skin and nail examination in primary care is crucial in distinguishing DD from more common conditions and avoiding unnecessary treatments [2, 10].

In many primary care settings, the absence of facilities for skin biopsies and histopathological analysis further complicates the diagnostic process. A definitive diagnosis of DD is confirmed by histopathological findings, which typically show suprabasal acantholysis, dyskeratotic cells (corps ronds and grains), and hyperkeratosis [2, 6]. However, PCPs often have limited access to technical procedures and leading to prolonged dependence on empirical treatments. As relapsing nature of DD, recognizing the failure of conventional therapy, referring patients to dermatology for further evaluation are essential in achieving timely diagnosis and intervention.

Several non-invasive imaging techniques have also been described in the literature as valuable adjuncts for diagnosing DD. For example, dermoscopy can reveal distinctive features such as yellowish-brown polygonal keratotic areas with central depressions and a “cracked riverbed” appearance [11]. Reflectance confocal microscopy (RCM) offers real-time, in-depth imaging of the skin, allowing visualization of intraepidermal lacunae and dyskeratotic cells, while optical coherence tomography (OCT) can highlight hyperkeratosis and acantholysis. High-frequency ultrasound has also been used to identify epidermal thickening and small fluid-filled spaces that correspond to vesicles or erosions [12]. These non-invasive techniques can aid in supporting early diagnosis. However, in our clinical practice setting, these advanced imaging modalities such as RCM, OCT, and high-frequency ultrasound are not available. Dermoscopy remains the only accessible tool for non-invasive skin assessment. A cross-sectional study in [13] found that steroid-dependent or damaged facial skin often shows dermoscopic pattern such as polygonal vessel and depigmentation that may mimic rare dermatoses like DD and further complicating clinical recognition. In this particular case, dermoscopy was not performed, and we proceeded directly to skin biopsy in view of DD is a rare condition listed in Malaysia’s registry of rare diseases, and considering the need for diagnostic certainty, histopathology remains the gold standard in our clinical setting to confirm the diagnosis. Expanding access to advanced non-invasive diagnostic tools in primary and hospital care settings could help improve early detection of DD and may reduce the need for invasive procedures like biopsies in the future.

Early recognition of red flags in skin lesion primary care can facilitate timelier referral and features such as treatment-resistant pruritic papules, nail dystrophy, and a positive family history should raise suspicion for DD [3, 5]. By the time standard eczema treatments fail to provide sustained relief, PCPs should have a low threshold for seeking dermatological input. Identifying DD early is crucial, as patients who remain undiagnosed may experience progressive skin involvement include frequent flare-ups, and prone to secondary infections, which significantly impact quality of life [6, 9].

Although systemic treatment for DD, such as oral retinoids (acitretin, isotretinoin), is typically initiated by dermatologists, PCPs play a crucial role in symptom relief and patient education [4]. Patients should be advised on trigger avoidance, including protection against heat, ultraviolet exposure, excessive sweating, and mechanical friction, which can exacerbate symptoms [2, 7]. Supportive treatments such as topical keratolytic (10% urea cream, lactic acid), emollients, and oral antihistamines can help alleviate symptoms while awaiting specialist input.

While topical corticosteroids are a mainstay in the symptomatic management of DD, particularly for reducing inflammation and controlling flare-ups, prolonged or inappropriate use can lead to a range of adverse effects. These include skin atrophy, telangiectasia, striae, hypopigmentation, and, in some cases, tachyphylaxis, where the treatment becomes less effective over time [13-15]. Prolonged application, especially of potent steroids on delicate skin areas, increases the risk of these complications. In our patient’s history, despite long-term use of topical corticosteroids for presumed eczema, there was minimal symptom relief, underscoring the importance of revisiting the diagnosis when standard treatments fail. Although no specific adverse effects from long-term corticosteroid use were documented in this case. Particular caution is needed for facial applications, which have been associated with steroid-induced rosaceiform dermatitis which are characterized by erythema, burning and popular flares as documented in [15]. This highlights the need for regular monitoring and careful counselling on the risks of prolonged steroid use, especially when patients are not responding as expected. Furthermore, Cochrane reviews on topical anti-inflammatory agent for seborrheic dermatitis remind us that although corticosteroid may help in short term inflammation control, their prolonged use without definite diagnosis may delay appropriate management of rarer disease such as DD [14].

The pathophysiology of pruritus in DD is complex and involves more than just histamine-driven pathways. A key factor is the skin barrier dysfunction caused by mutations in the ATP2A2 gene, which disrupts keratinocyte adhesion and weakens the epidermis. This leads to increased transepidermal water loss and exposes peripheral nerve endings, making the skin more sensitive and prone to itch. In addition, chronic inflammation that triggered by release of cytokines like IL-31, TNF-a and IL-6 may worsen the itchiness. Due to its overlapping mechanisms, antihistamines are often partially effective in managing the symptoms [16]. In our case, we prescribed loratadine, a second-generation H1-antihistamine with a mechanism similar to cetirizine, to help relieve the patient’s itch. This reflects the broader class effect of H1-antihistamines, however, as expected, the response was limited due to the multifactorial nature of pruritus in DD. While literature highlights the use of antihistamines for relieving burning sensations, the same therapeutic approach can also benefit pruritus, as both symptoms share similar underlying pathways. Therefore, comprehensive management including treatments that strengthen the skin barrier and reduce inflammation are essential for better symptom control.

It is also well recognized that DD can affect not only physical health but also mental and emotional well-being. Many patients experience low self-esteem, social withdrawal, anxiety, and depression due to the chronic, visible, and often stigmatizing nature of their skin lesions [17]. In our case, the patient had been living with visible skin lesions since his teenage years, involving areas such as the face, neck, and upper torso, and had experienced decades of persistent symptoms despite multiple treatments. Although he did not explicitly report psychological distress, the prolonged course of the disease, its visible nature, and his history of treatment failure likely had an emotional and social impact. To better understand the patient’s perspective and assess the overall

effect of skin disease on daily life, tools like the dermatology life quality index (DLQI) are especially useful. The DLQI is a widely validated questionnaire that helps quantify how much a skin condition affects daily activities, emotional well-being, and social interactions, offering valuable insight for more holistic, patient-centered care [18]. Although the DLQI was not performed in this case, its use is recommended in future clinical practice to capture the full burden of disease and guide tailored management.

Furthermore, PCPs must be prepared to monitor adverse effects of systemic retinoids, including dry skin, mucosal irritation, and hepatotoxicity, ensuring that patients receive holistic, long-term care in collaboration with dermatologists [7, 8].

DD, though rare, has a significant impact on patients' quality of life and often remains undiagnosed or mismanaged in primary care. Since PCPs are usually the first healthcare providers to assess skin conditions, maintaining a high index of suspicion for DD in cases of chronic, atypical, treatment-resistant skin lesions is vital [8, 9]. Timely recognition and referral can prevent years of unnecessary treatment, reduce patient distress, and improve long-term disease control. Additionally, recent case reports have highlighted how certain immunosuppressive and targeted treatments in other skin diseases may paradoxically worsen or unmask underlying conditions. The study in [19] describes such immunological paradoxes in psoriasis and rheumatoid arthritis, which underscore the need for clinical vigilance when expected responses fail. By equipping themselves with a better understanding of this condition, PCPs can play a pivotal role in enhancing early diagnosis, optimizing treatment pathways, and ultimately improving patient outcomes.

CONCLUSION

DD is a rare condition that is often misdiagnosed, particularly in primary care settings where it is frequently mistaken for eczema or seborrheic dermatitis. Given its chronic and treatment-resistant nature, early recognition is crucial to prevent prolonged ineffective management and unnecessary distress to the patient. PCPs should maintain a high index of suspicion when encountering triad of persistent pruritic papules, nail abnormalities, and a positive family history of DD despite an empirical treatment of eczema or seborrheic dermatitis. Prompt and timely referral for dermatological assessment and histopathological confirmation are crucial in further management plans. While systemic retinoids remain the mainstay of DD treatment, primary care providers play a critical role in patient education, symptom management, and long-term disease monitoring. This case underscores the importance of clinical vigilance in primary care, ensuring earlier diagnosis and appropriate intervention, and helps improve quality of life of affected individuals.

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Declaration of interest: No conflict of interest is declared by the authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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