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Diagnosis and management of vulvar Darier disease: A case report

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ABSTRACT

Darier disease is an autosomal dominant disorder with hyperkeratotic papules affecting primarily seborrheic areas of the upper chest, back, forehead, scalp, nasolabial folds, ears, and, less frequently, the oral mucosa. A typical eruption consists of keratotic and crusted skin-colored papules and plaques. Pruritus occurs in 80% of patients, and pain is rare. Lesions can be triggered by exposure to ultraviolet light, heat, or stress. Secondary infections of the lesions are a common complication. A definitive diagnosis is obtained by a biopsy showing histological features such as acantholysis, suprabasal clefts, and "corps rond and grains". Here we present a 37-year-old woman admitted to the gynecology department with pruritic lesions she had noticed on her vulva and perineum for three months. A vulvar biopsy led to the diagnosis of Darier disease. She was referred to the dermatology department and treated with oral acitretin since systemic retinoids are offered as the first-line treatment of the disease.

1. Introduction

Darier disease, also known as keratosis follicularis, was initially described by Jean Darier and James Clark White in 1889 [1]. It is a rare form of autosomal dominant genodermatosis with a prevalence of about 1:30,000–1:100,000. The autosomal dominant inheritance of the disease was described in 1999 when Sakuntabhai et al. identified the ATP2A2 gene, which encodes the type2 Sarco (*endo*)-plasmic reticulum Ca + 2-ATPase (SERCA2), as the causative gene for Darier disease [2]. SERCA2 abnormalities can negatively affect the adhesion of keratinocytes, also the synthesis and proper formation of desmosomal components, leading to dyskeratotic and parakeratotic cells [3].

Darier disease is characterized clinically by crusted, skin-colored hyperkeratotic papules that may coalesce in plaques. The lesions typically involve the seborrheic areas, including the scalp, forehead, upper chest and back. Mucous membranes are affected in 15% of patients [4]. The disease rarely affects the vulva.

Darier disease can be distressing, as it can cause significant discomfort and affect the patient's appearance. We present a rare case of Darier disease involving the vulvar area, which was treated with oral retinoids, resulting in symptom relief.

2. Case Presentation

A 37-year-old woman presented to the gynecology clinic for an itchy, erythematous rash on her vulva, perineum, and groin that had been present for over three months. She had experienced similar symptoms since she was 24, but the lesions had typically resolved without treatment. The affected area was more extensive than before, and she reported vulvar pain. She had no concurrent medical conditions, did not smoke, and had a body mass index (BMI) of 35. There was no family history of skin disease, and no other family members reported similar symptoms.

On physical examination, pruritic hyperkeratotic papular lesions were noted diffusely on the vulva and perineum (Figs. 1 and 2). Papules were also present on her forehead and axillary area (Figs. 3 and 4). The patient also had crusted, coalescing areas on her upper chest and gluteal region (Figs. 5 and 6). The oral mucosa appeared normal. The patient reported that she first noticed the lesions on her upper chest at the age of 20 and that they would come and go without treatment. The patient emphasized that the lesions were triggered by heat and aggravated during spring and summer.

A vulvar biopsy was performed under local anesthesia, and the sample was subjected to histopathological examination, which revealed hyperkeratosis with parakeratosis on the surface, acanthosis, and

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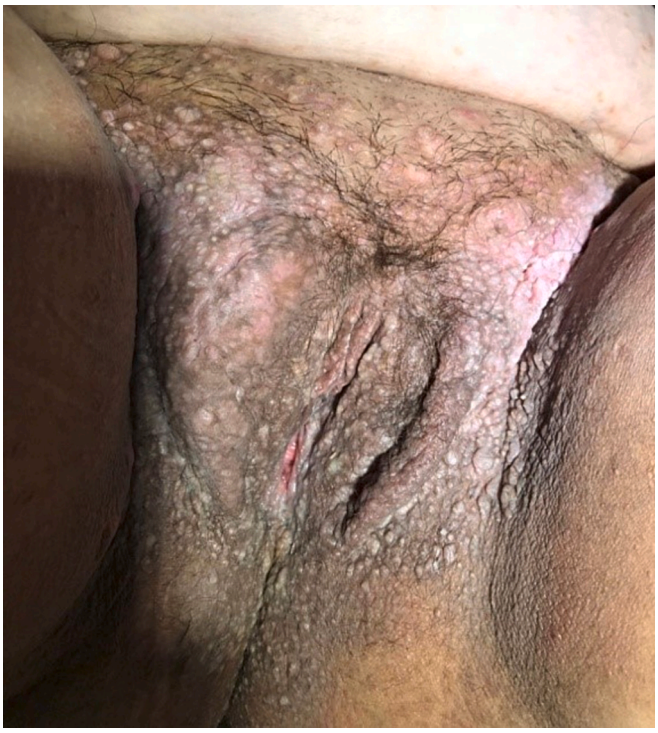

Fig. 1. Lesions on the vulva.

acantholysis in the epidermis (Fig. 7. a and b). Upon closer view, dyskeratotic cells, depicted as "corps ronds" in the upper layers of the epidermis and "grains" in the stratum corneum, were observed (Fig. 7. c and d). Findings were consistent with a diagnosis of Darier disease.

The patient was then referred to the dermatology department for further evaluation and was officially diagnosed with Darier disease. The patient was prescribed 25 mg/d of acitretin, and a marked improvement in the lesions was immediately observed. The patient remained asymptomatic while on acitretin at her one-year follow-up.

3. Discussion

Darier's disease is a rare genodermatosis, usually transmitted in an autosomal dominant pattern. ATP2A2 gene mutations are known to be the cause of the condition [5]. As a result of the ATP2A2 gene mutation, impaired keratinocyte adhesion and also dyskeratotic and parakeratotic cells are seen histologically.

Even though it is known to be an autosomal dominant disorder, about 47% of patients do not report a family history of the condition [6]. The present patient also had no known family history, which can be explained by new sporadic mutations or mild forms not recognized among family members. Therefore, patients should receive genetic counseling with information about the risk of transmission to the offspring.

Darier disease has a chronic course with frequent relapses. The triggering factors of the disease include stress, exposure to ultraviolet light, heat or infection [7]. The patient first noticed her lesions at 22 years of age. They were aggravated by exposure to heat; therefore, the lesions worsened during spring and summer. Characteristic skin lesions are hyperkeratotic papules and plaques primarily affecting seborrheic areas. The genital tract is an unusual region for the disease to affect.

Individuals with Darier disease often present with pruritus and pain. The vulva was the most affected area in the present case, followed by the forehead, scalp, axillary region, upper chest, and gluteal area. Vulvar pruritus and pain were the causes of admission.

A biopsy of the affected area is necessary to confirm the diagnosis. The main histologic features of Darier disease are acantholysis and dyskeratosis. Dyskeratotic cells described as 'corps ronds', and parakeratotic cells described as 'corps grains', are the characteristic histologic findings of the disease [8]. The histopathological appearance also supported the diagnosis in the present case.

Darier disease is included in the group of dyskeratotic acantholytic dermatoses along with Hailey-Hailey disease, Warty dyskeratoma, and acantholytic dyskeratotic acanthoma. These diseases share features like acantholysis and dyskeratosis, the result of abnormal keratinization [9].

Unlike Darier disease, pruritus is less common and the scalp is less commonly affected in Hailey-Hailey disease. The patient complained of itchy, crusted lesions on the vulvar area; her forehead and scalp were also affected with similar lesions [10]. While both diseases are characterized by multiple lesions affecting the body, warty dyskeratosis and acantholytic dyskeratotic acanthoma, which have unclear pathogenesis, typically present as localized single lesions [11]. In the differential diagnosis, consideration should also be given to acantholytic dermatosis of the genitocrural area, also known as papular acantholytic dermatosis of the vulva-crural area. This disease is limited to these regions and is thought to be a localized form of Darier [12].

The main aim of treatment for Darier disease is to relieve the symptoms and improve the patient's quality of life. Several treatments are presented in the literature, such as sunblock and antiseptic emollients, avoidance of the triggering factors, topical retinoids, and topical steroids; they provide benefits in mild to moderate types of Darier disease. Barrett et al. reported a case of a woman with vulvar pruritus that was later diagnosed as Darier's disease. The lesions were mainly in the vulvar area; therefore, topical corticosteroids were effective in resolving the symptoms [13].

Systemic retinoids, such as isotretinoin and acitretin, are the first-line treatment in all patients and are effective in 90% of cases [14]. They act by suppressing acantholysis and dyskeratosis; they also induce cell proliferation, keratinization, and immunomodulation, resulting in relief of the symptoms. Mansouri et al. reported a case of a woman with hyperkeratotic papules on the vulva [15]. A skin biopsy was performed for the diagnosis, and the pathology report was consistent with Darier disease. The patient was treated with oral acitretin. The patient's symptoms resolved entirely after treatment, and no recurrence was seen in her follow-ups.

Treatment duration should be adapted to the clinical response. In women of childbearing age, teratogenicity is a significant consideration for acitretin treatment.Women should be advised to avoid pregnancy

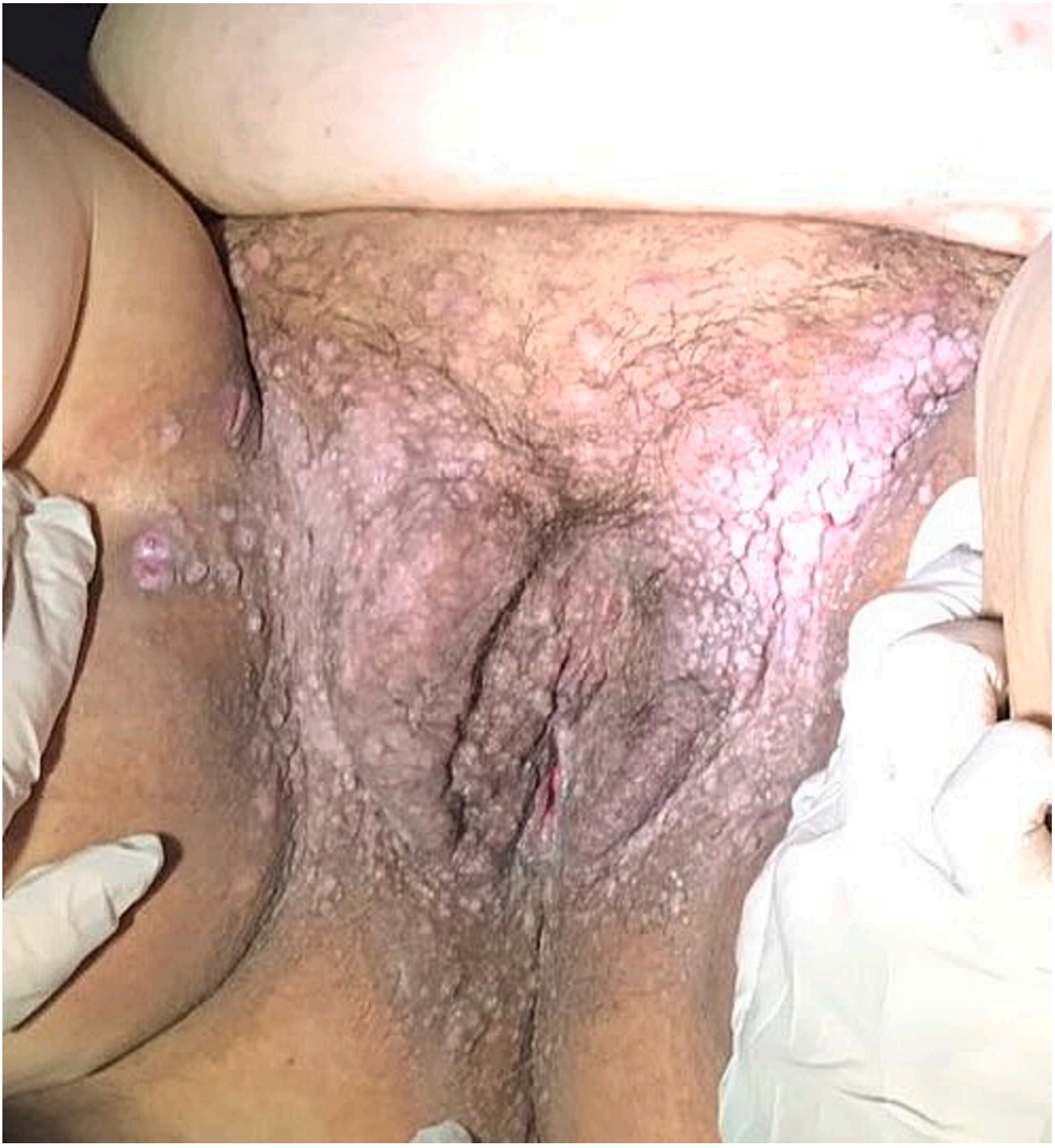

Fig. 2. Papules and plaques on the vulva.

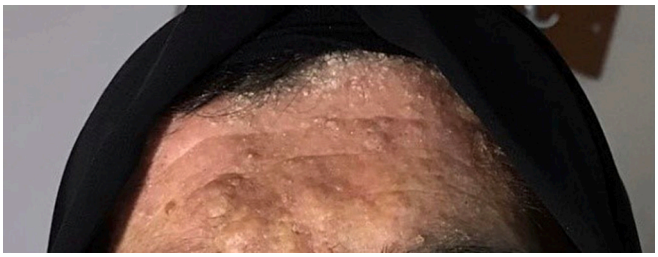

Fig. 3. Lesions on the forehead.

during treatment and for at least two years after discontinuing acitretin. The patient in this case was treated with 25 mg/daily oral acitretin, which was well tolerated with no side-effects and effectively controlled the disease. Understanding the clinical characteristics and underlying genetic cause of Darier disease is significant for accurate diagnosis and management of affected patients. With proper management, individuals with the condition can lead fulfilling lives.

Contributors

Ipek Evruke contributed to conception of the case report, patient care, acquiring and interpreting the data, undertaking the literature review and drafting the manuscript.

Funda Gungor Ugurlucan contributed to patient care, conception of the case report and acquiring and interpreting the data.

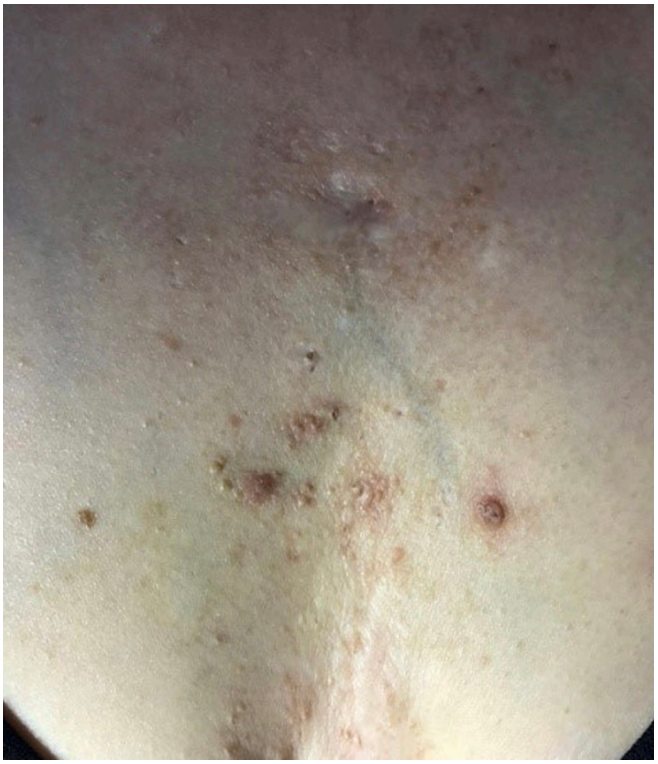

Fig. 5. Hyperkeratotic papules on the chest.

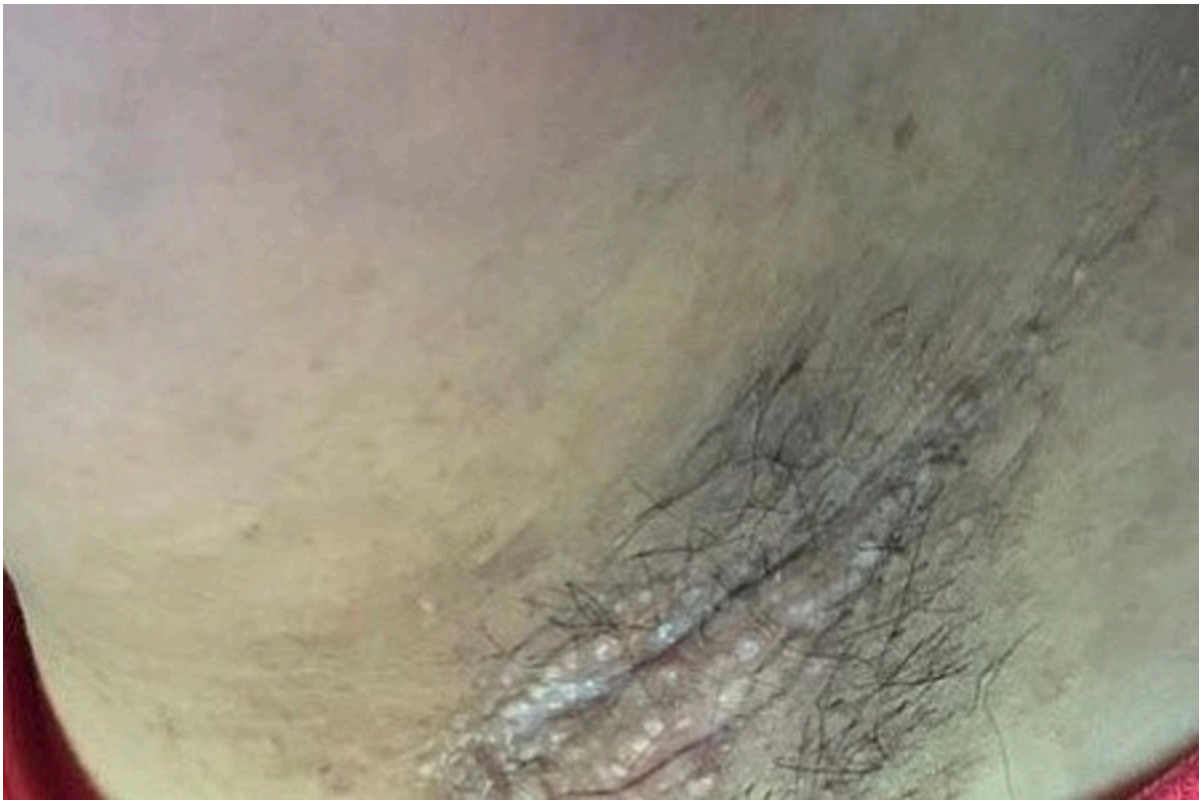

Fig. 4. Papules on the axillary area.

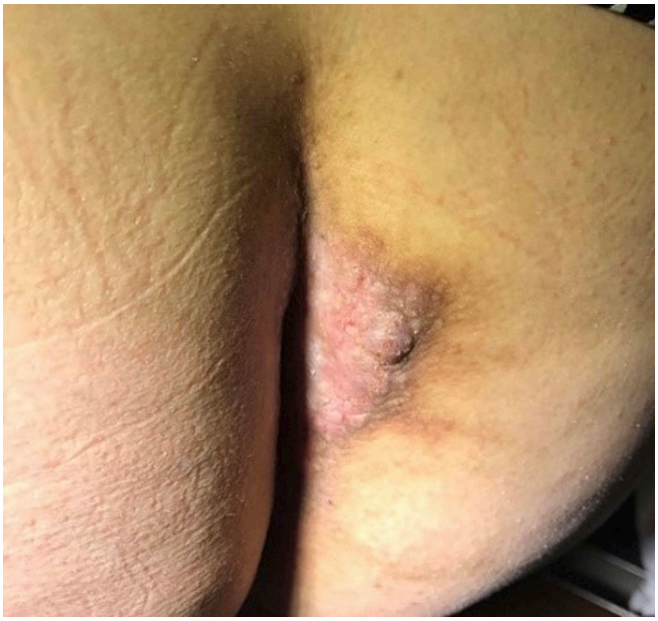

Fig. 6. Hyperkeratotic papules on the gluteal area.

Begum Yeni Erdem contributed to acquiring and interpreting the data, drafting the manuscript and undertaking the literature review.

Sule Ozturk Sari contributed to drafting the manuscript and undertaking the literature review.

All authors contributed to revision of the manuscript and approved the final submitted version.

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Patient consent

Consent was obtained from the patient to publish the clinical details and images included.

Provenance and peer review

This article was not commissioned and was peer reviewed.

Conflict of interest statement

The authors declare that they have no conflict of interest regarding

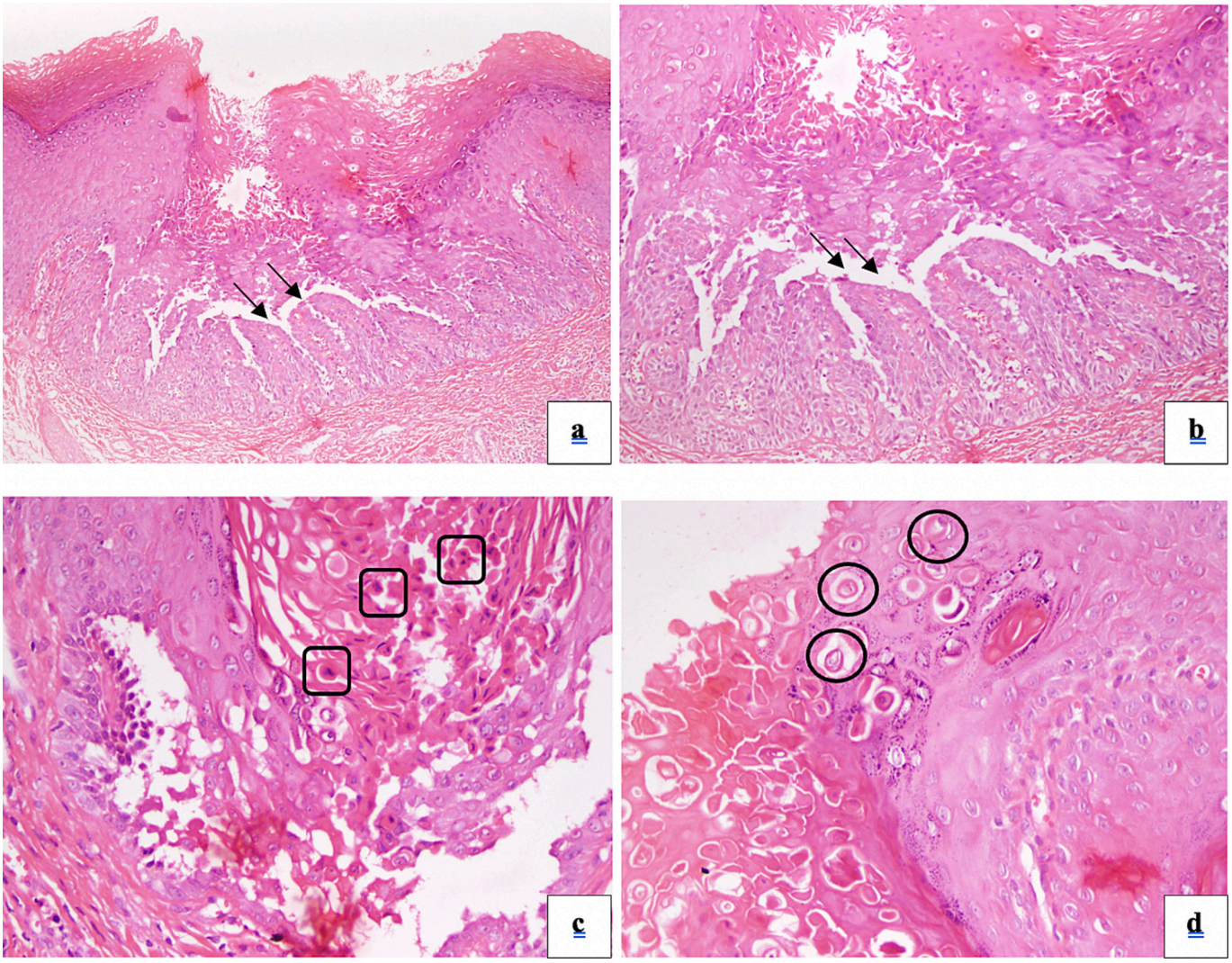

Fig. 7. (a-d) Hematoxylin-eosin stained sections. a. Low power view of the lesional biopsy. Keratotic tier can be seen on the top. Marked acanthosis and a suprabasal acantholytic area (arrows) is seen in the epidermis. b. Closer view of the acantholytic area. A suprabasal cleft (arrows) is formed. c. Dyskeratotic cells in the form of "grains" can be seen in the keratotic tier (highlighted by squares), d. Dyskeratotic cells in the form of "corps ronds" can be seen in the granular layer of the epidermis (highlighted by circles).

the publication of this case report.

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