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Coexistence of Darier's disease with acrokeratosis verruciformis of Hopf: A case report

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Abstract:

In this case study, we reported a case of a 23-year-old female with both Darier's disease (DD) and acrokeratosis verruciformis of Hopf (AKV), two rare autosomal dominant skin disorders that are differentiated clinically and histopathologically but are both caused by a single gene mutation, i.e., ATP2A2 on chromosome 12, which is expressed in the skin. Patient was presented with multiple hyperpigmented lesions all over body from past 11 years. The biochemical investigations revealed to be in physiological range. The patient was successfully managed by oral isotretinoin.

Introduction

Darier's disease (DD), also known as Darier–White disease, is an autosomal dominant genodermatosis that is typified by alterations in the mucous membranes and nails as well as greasy hyperkeratotic papules in the seborrheic region. DD is associated with a mutation in the ATPA2 gene was first identified by Prince Marrow in 1886 and separately reported by Darier and White in 1889 (1). Infections, heat, friction, and sunshine all make DD severe. Usually appearing around puberty and continuing throughout life, the clinical appearance includes many red or brown papules with hyperkeratosis, nail abnormalities such as longitudinal erythronychia, and mucosal modifications. DD is an uncommon disorder that

affects males more often than women, with an incidence of one case per 100,000 (2).

The uncommon genodermatosis known as Acrokeratosis verruciformis of Hopf (or just AKV) is typified by keratotic lesions on the dorsum of the hands and feet. Although it can sometimes occur as late as the fifth decade, AKV most frequently manifests in early childhood. The illness has a chronic course with no spontaneous remission. It has partial penetrance and an autosomal dominant inheritance pattern. There may not always be a family history. There is no preference for one gender over another. In 1931, Hopf published the first description of AKV (3). A mutation in the ATP2A2 gene, which is found on chromosome 12q24 and is also impacted in Darier disease, is the most likely cause. Although they are separate conditions, a patient may have both of them (4).

Clinically, flat-topped keratotic papules and plaques on the dorsum of the hands and feet are indicative of Hopf's acrokeratosis verruciformis. Lesions may less commonly appear on the arms or legs. Sebaceous regions such as the oral mucosa, flexural surfaces, and frontal scalp are unaffected by the illness. Leukonychia, longitudinal ridges, and thickening of the nail plate are some of the related nail abnormalities. The lesions will exhibit hyperkeratosis, hypergranulosis, papillomatosis, and acanthosis on histopathology. There is no parakeratosis in the lesions (3). Many physical and chemical factors such as phenol, ultraviolet B, heat, ethyl chloride spray, and lithium have been reported to exacerbate this disease (5).

The link between DD and AKV is still debatable. Some researchers had proposed that AKV and DD were clinically and histologically separate entities prior to the introduction of genetic testing methods, while others thought they were different manifestations of the same illness (6, 7). However, it has been shown that AKV is really an allelic variation of DD because to the availability of genetic testing methods. In addition to AKV, DD is brought on by a mutation in the gene that codes for sarco/endoplasmic reticulum Ca2+ ATPase. There have been isolated reports of each ailment, and a patient may have both conditions at the same time (8).

The symptoms of AKV might be mistaken for plane warts, seborrhoeic keratosis (SKs), DD, and epidermodysplasia verruciformis (EV). A histological investigation is typically necessary for differential diagnosis in order to rule out these possibilities. Hyperkeratosis, hypergranulosis, acanthosis, and confined elevations of the epidermis that resemble church spires are visible in the histopathology of AVH (4). We present a case of DD with AKV.

Case report

The case was a 23-year-old female presented to Dermatology OPD with multiple hyperpigmented lesions over face, B/L hands, B/L feet, and hypopigmented lesions over abdomen from past 11 years. On examination Multiple discrete skin coloured to hyperpigmented papules of size 0.6 * 1 cm, round to oval in shape over dorsum of hands, B/L feet, face, neck and forehead and multiple diffuse hypopigmented macules present over abdomen and upper back of size 0.3*0.5 cm, round to oval in shape (Figure 1).

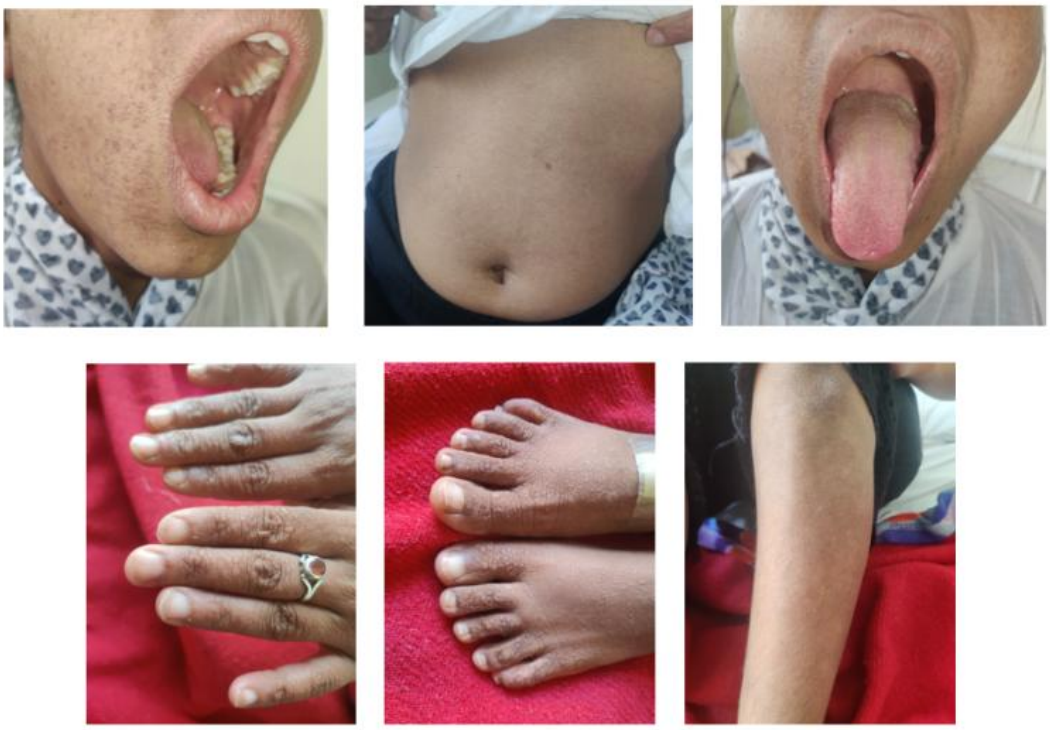

Figure 1: ***Multiple presented with discrete skin coloured to hyperpigmented papules over dorsum of hands, B/L feet, face, neck and forehead and multiple diffuse hypopigmented macules over abdomen and upper back.***

Complete blood count, liver functions, kidney functions, and blood sugar were all within the normal limits. Skin biopsy revealed acanthosis, hyperkeratosis, parakeratosis, and acantholytic cleft at the suprabasal level. On higher magnification, dyskeratotic cells (corps ronds and grains) were visible. Dermis showed perivascular and periadnexal lymphocytic infiltrate. Skin biopsy from the dorsum of the hand revealed papillomatosis (church spire appearance), hyperkeratosis, and hypergranulosis without acantholysis or dyskeratosis (Figure 2).

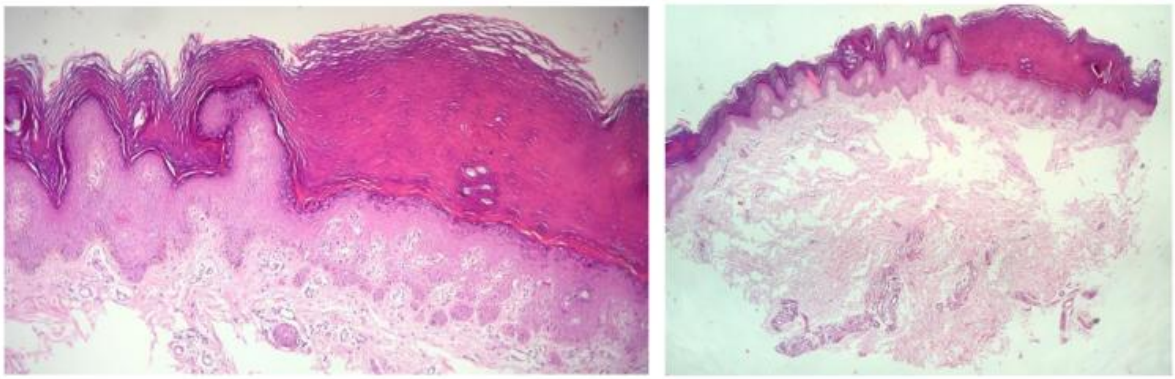

Figure 2: ***Histopathological examination showing hyperkeratosis and church spires.***

The current exacerbation was successfully managed by oral isotretinoin and showed improvement within 2 weeks of commencing treatment. Sebaceous glands are impacted by the oral prescription drug isotretinoin, which is used to treat severe acne. The US Food and Drug Administration (FDA) authorized the medication in 1982 to treat severe, resistant nodular acne that did not improve with systemic antibiotics or other traditional forms of treatment.

Discussion

The sarcoplasmic endoplasmic reticulum Ca2+ ATPase type 2 protein (SERCA2) is encoded by the ATPA2 gene, located at chromosome 12q23–12q24. A mutation in this gene causes DD, a rare autosomal dominant genodermatosis. The primary function of SERCA2 is to move Ca2+ from the cytosol to the endoplasmic reticulum lumen (9). When SERCA2 is defective, the cell membrane lacks Ca2+, which impairs cell-to-cell adhesion and causes apoptosis (10). This condition affects 1 in 100,000 people in the population. Although the incidence is the same for both sexes, males seem to be more negatively impacted than females (11). However, in our case report, the patient presented with the disease was a 23-year-old female.

The appearance of many, hyperkeratotic papules dispersed across seborrhoeic regions, as in our case, is one of the clinical characteristics of DD. Additional clinical features include the distal wedge-shaped nail plate, palmer plantar pits with red and white longitudinal bands, cobblestone papules on the oral mucosa, flexural vegetative lesions, and wart-like papules on the dorsal side of the hands and feet. Due to bacterial contamination, the patient may also exhibit an unpleasant odour. Lesions are often asymptomatic, and 50% of cases involve the oral mucosa (12).

Mutations in ATP2A2 have been found in AKVH patients, indicating that this illness may represent a variation of DD. The idea that AKV and DD are distinct conditions or components of the same disease process has been contested for many years. The occurrence, as in this family, of pure pedigrees whose individuals exclusively possess AKV traits serves as the primary justification for AKV and DD being distinct entities. The existence of mixed pedigrees supports the idea that AKVH is a component of the DD spectrum, and it is noteworthy that 50% of DD patients exhibit acral warty papules, which are indicative of AKVH. Multiple flesh-colored, flat-topped papules on the hands and feet, punctate keratosis on the palms and soles, and varied nail involvement are its defining features (8). Similar lesions that are indicative of AKVH are seen on the dorsum of hands in present case.

Acantholysis and dyskeratosis, which are characterised by "corps ronds" and "grains," are histopathological hallmarks of DD. Corps ronds are centre round dyskeratotic basophilic masses with a distinct halo-like zone surrounding them in the granular cell layer of the epidermis. Desmosome loss, keratin intermediate filament attachment breakage, and perinuclear aggregation of keratin intermediate filaments are all demonstrated by electron microscopy. Acanthosis, hyperkeratosis, hypergranulosis without parakeratosis, and papillomatosis with confined epidermal elevations known as "church spire" are histopathological characteristics of AKVH (13). The histopathology findings of present case were consistent with AKVH.

The absence of proven curative therapy protocols makes treating DD difficult. Systemic/topical retinoids, corticosteroids, cyclosporine, fluorouracil, derma-abrasion, electrosurgery, ablative lasers, photodynamic therapy, and surgical excision are among the therapeutic techniques that have been documented in the literature; nevertheless, their efficacy is limited. Ninety percent of individuals have shown some improvement in their symptoms while using systemic retinoids. They smooth papules, lessen odour, and lessen hyperkeratosis. As a result, our patient responded well to isotretinoin. Emollients and sunscreen are also essential. As a result, it's critical to guarantee a multidisciplinary approach while treating individuals with DD (14).

The absence of genetic, molecular, and functional investigations to validate and connect the allelic similarities between DD and AKVH are primary limitation of our case, despite the fact that our clinical picture and histologic findings corroborate it.

Conclusion

The patient should get genetic counselling that includes information on the hereditary illness and the risk of transmission to the offspring, regardless of the clinical severity and available treatment options. In order to make a conclusive diagnosis based on this outcome, a biopsy is essential. Patients should be made aware of the care needed and the complications associated with this illness. A multidisciplinary team should treat these individuals.

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