Case Report

Co-Existence of Darier Disease and Acrokeratosis Verruciformis of HOPF

Sadaf Ahmed Asim[1], Sania Imtiaz[2], Sharmeen Nasir[3]

Abstract

We report a case of 17-year-old girl who has both Darier's disease (DD) and Acrokeratosis verruciformis Hopf (AKVH). These two conditions have a similar pattern of inheritance and share clinical characteristics. The girl presented with skin-colored papules on her hands and feet since age of 6 years and recently developed violaceous papules in the axilla, umbilicus and trunk. This article highlights the rarity regarding the co-existence of both DD and AKVH.

Received: 27-12-2023 **Revision:** 30-05-2024 **Accepted:** 05-09-2024

Author's Affiliation:
[1-3]Department of Dermatology, Dow University Hospital Ojha, Karachi
Corresponding Author: Dr. Sania Imtiaz, Department of Dermatology, Dow University Hospital Ojha, Karachi
Email: Saniaimtiaz11@outlook.com

Introduction

Darier disease is an uncommon hereditary condition with a a prevalence of 1 case per 100,000 people and characterized by aberrant keratinization patterns, with an autosomal dominant mode of inheritance. It affects the seborrheic areas as well as the palms, nails, and oral mucosa. The lesions are firm, rather greasy, crusted papules that are skin-coloured to yellow-brown.[1]

Acrokeratosis verruciformis of Hopf is an uncommon autosomal genodermatosis, which is a hereditary skin disorder initially documented by Hopf in 1931. It is distinguished by the existence of flat, skin to reddish brown papules located on the dorsal surface of the hands and feet. These papules may also extend to the forearms, knees and elbows.[2]

In this particular case report, our objective was to thoroughly examine the clinical and histopathological findings of these two diseases, considering the most recent literature available.

Case Report

A 17-year-old girl presented with itchy skin-coloured to brownish papules on neck, axilla, umbilicus, trunk, hands, and feet since the age of 6 years. The patient had skin-coloured papules that initially first appeared over the dorsa of hands and feet followed by brownish to violaceous papules appearing on the axilla, neck and trunk. On dermatological examination: multiple, small, skin-coloured, flat-topped, papules were present over dorsa of hands and feet (Figure 1). Multiple, slightly violaceous, flat topped, papules were present over the axilla, inguinal crease, umbilicus, face upper chest, back, and abdomen (Fig. 2, 3, 4). No scalp, genital and oral mucosal lesions were observed. Nail examination revealed V-shaped nick on the nail of middle finger of the right hand (Fig. 5). She complained of aggravation of these lesions which was more prominent during the summer. Systemic physical examination and routine haematological and biochemical workup were within the normal limits.

Skin biopsies were taken from two different sites. Biopsy taken from abdomen shows Intra-epidermal blister which was suprabasal containing many acantholytic cells. Papillomatosis, acanthosis, hyperkeratosis with focal para-keratosis. cells with pyknotic nuclei were seen surrounded by a clear halo suggestive of corp rond. These findings were suggestive of Darier disease (Fig. 6). The biopsy taken from dorsa of foot revealed hyperkeratosis and papillomatosis with elevation

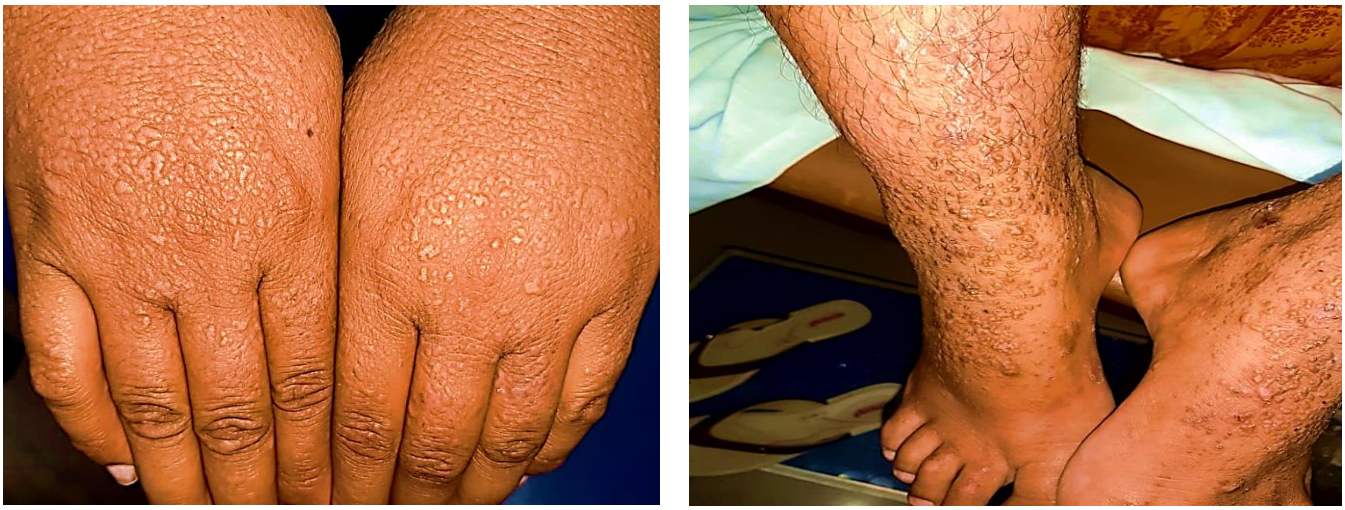

Figure 1: *Skin colored papules over dorsa of hands and feet.*

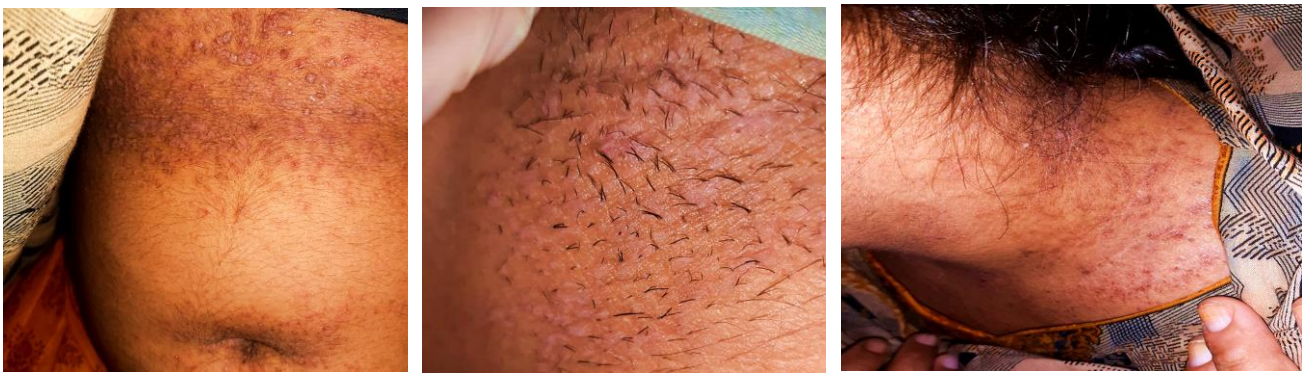

Figure 2, 3, 4: *Violaceous papules present over umbilicus, axilla and neck area.*

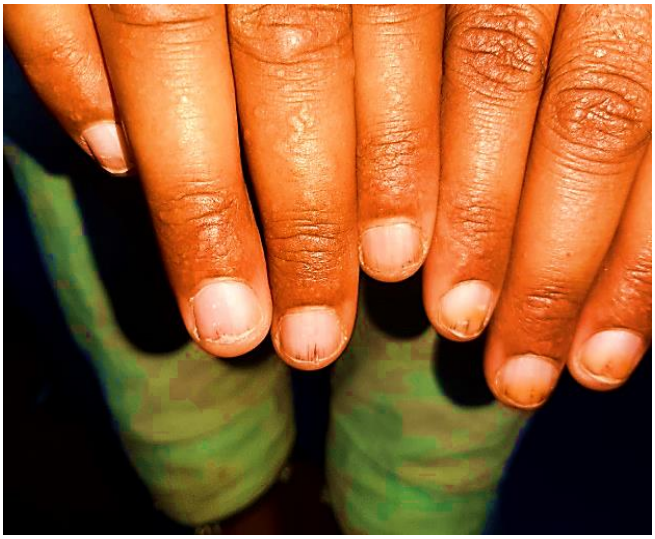

Figure 5: *V-shaped nick at middle finger of right hand.*

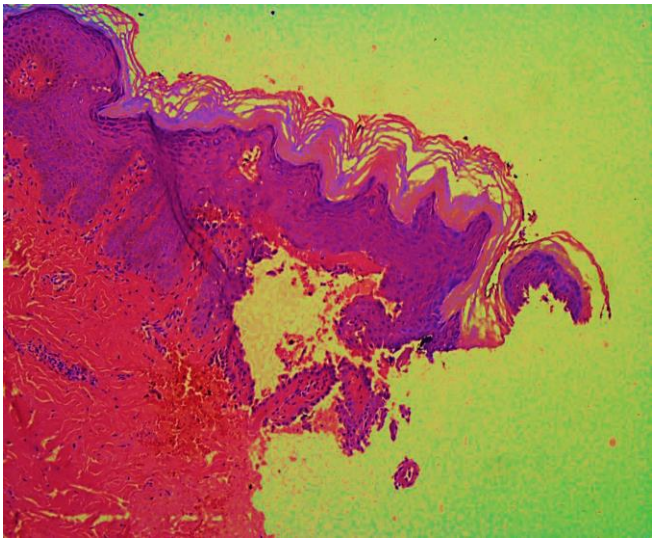

Figure 6: *Daries disease finding*

of epidermis resembling church spires and acanthosis, prominent granular layer. papillary dermis exhibited abundant collagen with vertically arranged collagen bundles. Mild perivas-

cular chronic inflammatory infiltrate seen. Features were suggestive of acrokeratosis verruciformis of Hopf (Fig. 7).

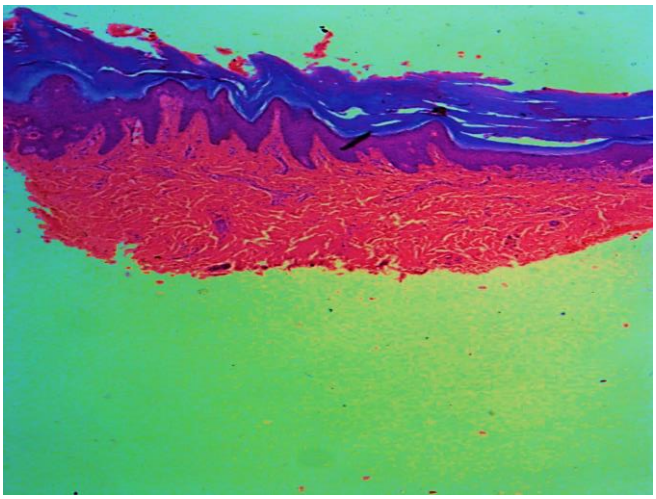

Figure 7: *Mile perivascular chronic inflammatory infiltrate*

The patient was counselled regarding the disease and she was treated with oral isotretinoin 20mg once daily, along with topical steroid and lactic acid, and sun protection. Cryotherapy was performed on the lesions affecting the hand and foot. With in a period of 6 weeks post-treatment, significant reduction in the size of the lesions was observed. The patient was closely monitored and received regular follow-up.

Discussion

The relationship between DD and AKVH has been debated for a long time. Both diseases are now believed to be caused by mutations in the same gene, ATP2A2, which encodes the SERCA2 pump, however, their histopathological features are different. Histopathological study showed similarities between AKVH and DD, suggesting they may be related disorders with variable expression of the same disease, although identical mutations n ATP2A2 have not been reported.[3]

The two diseases exhibit clinical similarities, however, in DD the acral lesions have a significant probability of transitioning into dyskeratosis at a later stage of life. Conversely, in AKVH the acral lesions remain non-dyskeratotic and non-acantholytic throughout the individual's lifespan. Essentially , the keratinization process in AKVH is exaggerated yet within normal parameters, whereas in DD it is intensified, modified and aberrant.[4]

DD is characterized by the presence of multiple, keratotic papules distributed in seborrheic areas. Additional features include wart-like papules over the dorsum of hands and feet, vegetative lesions on flexural areas, palmer and plantar pits, and nails exhibit red and white longitudinal bands, nail plate deformities in a distal wedge shape, and cobblestone papules on the oral mucosa. An offensive odor may also be experienced by the patient as a result of bacterial contamination. Approximately 50% of cases exhibit involvement of the oral mucosa, however, our patient does not display this particular feature.[5]

In AKVH, patient may exhibit the presence of conventional sin colored, flat, warty papules over the dorsum of hands and feet. Through careful examination, it is possible to identify the thickening of the skin on the palms and the soles, along with the occurrence of punctate keratoses. Furthermore, the nails display a whitish hue and an augmented thickness, accompanied by the presence of longitudinal ridges that fracture at the distal edge.[4]

The conclusive diagnosis of this condition relies on the observation of specific histopathological attributes, which encompass the manifestation of papillomatosis (characterized by circumscribed elevations of the epidermis commonly referred to as "church spires"), acanthosis, hyperkeratosis, and hypergranulosis, while parakeratosis is notably absent.[1,6]

The histopathological characteristics of DD encompass acantholysis and dyskeratosis which are manifest by the presence of "corps ronds" and "grain".

The management of DD continues to pose a significant challenge. Numerous treatment options have been documented in the literature including the use of sunscreen, topical retinoids, corticosteroid, cyclosporine, fluorouracil, systemic retinoids, dermabrasion, cryotherapy, ablative lasers, photodynamic therapy, and surgical excision. Nonetheless these interventions have

displayed limited efficacy. Notably, Systemic retinoids have proven emerged as a more effective option, leading to a partial alleviation of symptoms in 90% of patients. Consequently, our patient was administered isotretinoin, resulting in a favorable outcome.[5,7]

The only effective treatment for AKVH is superficial ablation. Other options are cryotherapy, laser therapy and surgical excision.[4,8]

Conclusion

In literature review very few cases of co-existence of DD and AKVH are reported, this case report was therefore presented due to its rarity. The case report highlights the clinical and histological features of both disease and the patient responded to oral isotretinoin Furthermore as a future perspective, AKVH may rarely transform to squamous cell carcinoma. Therefore, dermatology clinical professionals should cautiously monitor and educate patients diagnosed with AKVH.

Conflict of Interest: There was no conflict of interest to be declared by any author.

Funding Source: None.

Author's Contribution

SAA: Conceived, designed, edited the manuscript, final approval.

SI: Data collection and manuscript writing.

SN: Data collection and manuscript writing.

References

1. Piskin S, Saygin A, Doganay L, Kircuval D, Gurkan E. Coexistence of Darier's disease and acrokeratosis verruciformis of Hopf. Yonsei Med J. 2004;45(5): 956-9.
2. Verma J, Gopinath H, Josephain K, Bharti JN, Santosh T. Acrokeratosis Verruciformis of Hopf in an Adult - A Rare Case Report with Review of Literature. Indian journal of dermatology. 2022; 67(6):792-4.
3. Bergman R, Sezin T, Indelman M, Helou WA, Avitan-Hersh E. Acrokeratosis verruciformis of Hopf showing P602L mutation in ATP2A2 and overlapping histopathological features with Darier disease. Am J Dermatopathol. 2012;34(6):597-601.
4. Rallis E, Economidi A, Papadakis P, Verros C. Acrokeratosis verruciformis of Hopf (Hopf disease): case report and review of the literature. Dermatol Online J. 2005;11(2):10.
5. Paudel V, Pradhan MB, Shrestha B, Paudel S. Clinical and Histopathological Findings in a Patient of Darier-White Disease with Acrokertasosis Verruciformis of Hopf. Case Rep Dermatol Med. 2022; 2022:5233837.
6. Mohanty S, Panda S, Padhi S. Acrokeratosis verruciformis of Hopf: A rare case report. Indian Journal of Pathology and Oncology. 2023;10:108-11.
7. Haber RN, Dib NG. Management of Darier disease: A review of the literature and update. Indian J Dermatol Venereol Leprol. 2021;87(1):14-21.
8. Andrade TC, Silva GV, Silva TM, Pinto AC, Nunes AJ, Martelli AC. Acrokeratosis verruciformis of Hopf - Case report. An Bras Dermatol. 2016;91(5): 639-41.