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CASE REPORT

MVD Variants Identified in a Rare Clinical Variant of Porokeratosis: A Case Report of Disseminated Superficial Porokeratosis (DSP) in a Chinese Patient

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Abstract: Porokeratosis comprises a diverse range of both hereditary and acquired disorders characterized by clonal hyperproliferation of keratinocytes. These disorders manifest with a variety of clinical presentations but are histologically unified by the presence of the cornoid lamella. In this study, we report an unusual presentation of a rare clinical variant of porokeratosis, namely disseminated superficial porokeratosis, in which mutations in the Mevalonate decarboxylase (MVD) gene have been identified. This finding contributes to the growing understanding of the genetic underpinnings of this complex dermatological condition and may have implications for diagnosis and treatment.

Keywords: disseminated superficial porokeratosis, porokeratosis, MVD variants

Introduction

Porokeratosis is a rare dermatological condition characterized by abnormal keratinization, manifesting as raised keratotic papules or annular plaques. This diverse group of disorders encompasses several subtypes, including linear porokeratosis, porokeratosis of Mibelli, punctate porokeratosis, porokeratosis palmaris et plantaris disseminate, and disseminated superficial porokeratosis.[1] Additionally, there are other less common variants such as porokeratosis ptychotropica, facial porokeratosis, giant porokeratosis, hypertrophic verrucous porokeratosis, reticulate porokeratosis, and eruptive pruritic papular porokeratosis. Risk factors associated with the development of porokeratosis include genetic predisposition, immunosuppression, and exposure to ultraviolet light.

In this study, we present a unique case of a patient diagnosed with disseminated superficial porokeratosis, an uncommon variant of PK within this spectrum of disorders. We provide a comprehensive account of the clinical findings observed during routine examination, along with detailed dermoscopic and histological findings. This case report aims to contribute to the existing knowledge of porokeratosis, emphasizing its diagnostic challenges and the importance of a multidisciplinary approach (histopathology and genetics) in its management. By sharing our experience with this unusual case, we hope to enhance the understanding of porokeratosis among clinicians and researchers, ultimately improving patient outcomes.

Case Report

A 69-year-old Chinese male had a 50-year history of progressively spreading papules, which initially appeared on his upper limbs and later spread to involve his lower limbs, face, chest, and back bilaterally (Figure 1). These lesions measured between 1–5 mm in diameter and exhibited a brown coloration. Dermoscopic evaluation of a representative lesion revealed brown circular and dendritic structures superimposed on an erythematous background (Figure 2A), that could suggest a form of PK. He denied any similar skin manifestations among his family members.

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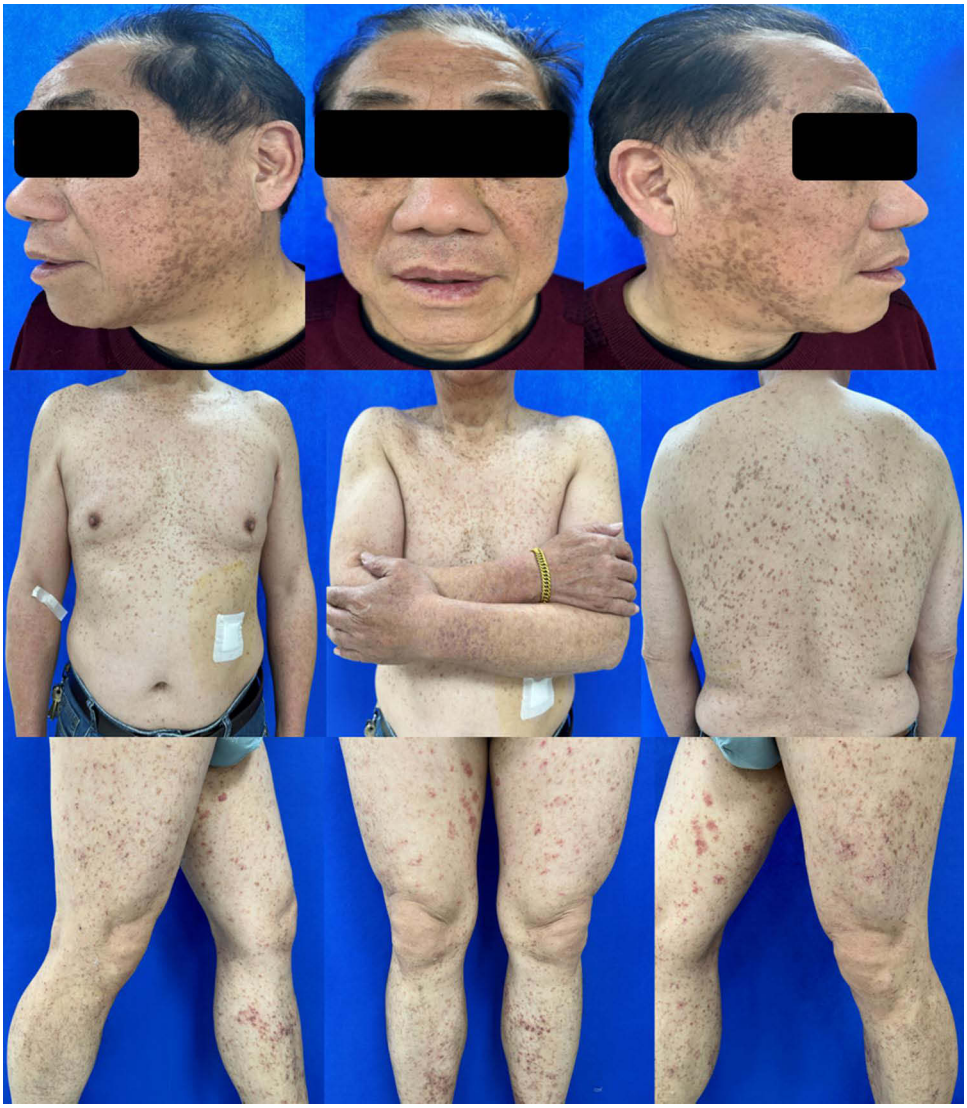

Figure 1 Clinical images showing polymorphic erythematous to-brown round lesions on the body of the patient.

To confirm the clinical suspicion, a histopathological examination was conducted. The results demonstrated diffuse parakeratosis with the presence of cornoid lamellae, acanthosis, and dyskeratotic cells within the epidermis. Furthermore, a band-like lymphocytic infiltrate was observed at the dermo-epidermal junction (Figure 2B). Additionally, a column of

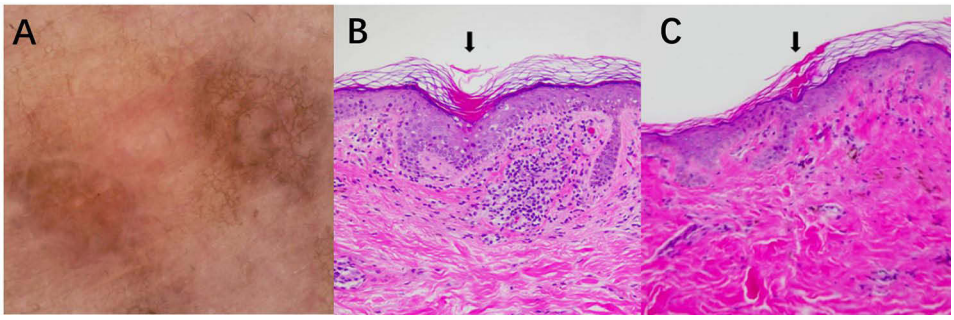

Figure 2 (**A**) Dermoscopy of the lesion corroborated the clinical features showing some brown circular and branched structures on an erythematous background. (**B**) Skin biopsy of the abdomen reveals some cornoid lamellae and intense hyperkeratosis, a perivascular lymphocytic inflammatory infiltration in papillary dermis (hematoxylin and eosin [H&E] stain). (**C**) A column of parakeratotic cells is seen correlating to the raised border of the lesion (hematoxylin and eosin [H&E] stain). The presence of the cornoid lamella, indicated by the black arrow, serves as a distinctive histopathological marker for all subtypes of porokeratosis.

parakeratotic cells was detected, which seemed to align with the raised perimeter of the lesion (Figure 2C). These findings were consistent with the diagnosis of Disseminated Superficial Porokeratosis (DSP).

The case report written informed consent was obtained from the patient, and the study was carried out after approval by the ethics committee of Hangzhou Hospital of Traditional Chinese Medicine and conducted according to the Declaration of Helsinki principles. To further investigate the genetic basis of this condition, Sanger sequencing was performed on DNA extracted from EDTA blood (Figure 3). PCR amplification of the relevant gene regions was carried out using standardized methods, followed by Sanger sequencing on an automated sequencer (ABI 3730xl; Applied Biosystems, Foster City, CA, USA). The sequencing results will provide additional insights into the underlying genetic alterations associated with this rare case of DSP.

Discussion

Porokeratosis (PK) is a genetically heterogeneous disorder characterized by distinct clinical phenotypes associated with mutations in specific genes involved in the mevalonate pathway. These genes include mevalonate decarboxylase (MVD), mevalonate kinase (MVK), phosphomevalonate kinase (PMVK), and farnesyl diphosphate synthase (FDPS).[2] Studies have demonstrated correlations between these genetic mutations and the resulting clinical manifestations of PK. Patients harboring MVK mutations typically exhibit a broad spectrum of phenotypes, distinguished by both the quantity and size of lesions, with diameters often exceeding 5 cm. In contrast, PMVK mutations appear to be uniquely associated with localized genital PK and porokeratoma phenotypes. Individuals with MVD mutations present with numerous lesions, generally measuring less than 2 cm in diameter. Lastly, patients with FDPS mutations typically manifest with a high number of lesions, exceeding 500 in most cases, and with lesion diameters under 1 cm.[3–5] These observations underscore the complex genetic architecture underlying PK and its diverse clinical presentations.

The lesions of Disseminated superficial porokeratosis (DSP) presents look similar to those in disseminated superficial actinic porokeratosis. However, a notable distinction lies in the absence of photo-distribution in DSP.[6] While DSP has been documented as an uncommon manifestation of the rare clinical variant of porokeratosis (PK), mutations in the mevalonate decarboxylase (MVD) gene have been exceptionally rare in previous case reports. We reviewed the clinical reports and studies on porokeratosis in the PubMed database and found that almost all patients with mutation at the MVD gene locus c.746T>C were accompanied by skin rashes affecting the entire body, and they were uniformly diagnosed with disseminated porokeratosis or disseminated actinic porokeratosis without exception. (Table 1).

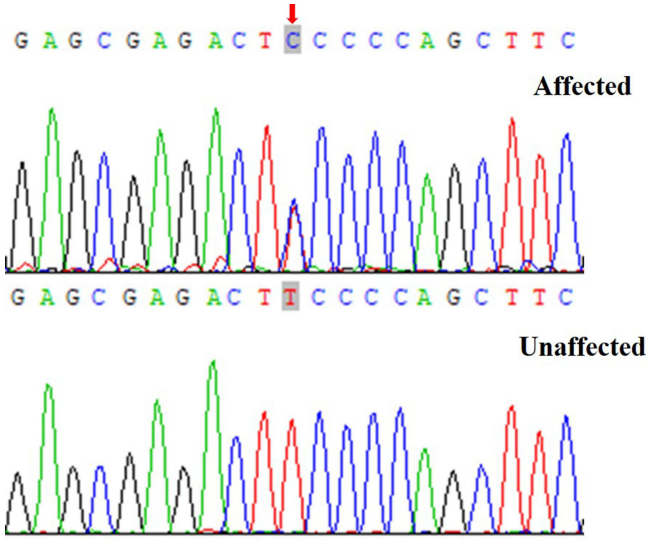

Figure 3 Sanger sequencing chromatograms of proband (patient with DSP, affected) and normal control (unaffected) at the c.746T>C mutation site indicated by arrow [NM_002461.3: exon7: c. T746C: p.F249S].

Table 1 Clinical Characteristics of Patients Carrying MVD Gene Mutations and Diagnosed with Porokeratosis

Patient	Sex	Age, years	Age of Onset	Porokeratosis Subtype	Rash Distribution Sites	Germline Mutation	History of Skin Cancer	References
1	Male	84	Preschool age	LP	Thorax\arm	c.70+5G>A	NO	Sabine JÄGLE et al[7]
2	Male	74	Babyhood	LP	Arm\hand\trunk\leg	c.70+5G>A	SCC	
3	Female	54	Childhood	LP	Arm	c.70+5G>A	NO	
4	Female	9	At birth	LP (systematized)	Face, trunk\legs\feet	c.70+5G>A	NO	
5	Male	65	18	DSP and Punctate porokeratosis of the palms and toes	Feet\hand\ ventral trunk	c.70+5G>A	NO	
6	Female	27	7	Porokeratosis plantaris	Feet	c.70+5G>A	NO	
7	Male	73	13	DSP and Punctate porokeratosis of the palms and toes	Feet\hand\ ventral trunk \ legs	c.70+5G>A	NO	
8	Male	36	18	DSAP	Upper and lower limbs	c.70+5G>A	NO	Lihi Atzmony et al[8]
9	Female	40	16	PPPD	Feet\ legs	c.70+5G>A	NO	
10	Male	53	19	PPPD	Feet\ legs	c.70+5G>A	SCC	
11	Male	78	NA	Sporadic porokeratosis	Extremities and trunk	c.1A>G (p.Met1?)	NA	Yuki ARISAWA et al[9]
12	Male	73	NA	Sporadic porokeratosis	Extremities and trunk	c.746T>C	NA	
13	NA	NA	NA	DSAP/DSP	Face, limbs, buttock, genitals	c.746T>C	NA	Yunji Leng et al[10]
14	NA	NA	NA	DSAP/DSP	Face, limbs, chest, buttock	c.746T>C	NA	
15	NA	NA	NA	DSAP/DSP	Face, chest, neck, limbs	c.746T>C	NA	
16	NA	NA	NA	DSAP/DSP	Face	c.1A>G	NA	
17	NA	NA	NA	LP	Face	c.1013+1G>A	NA	
18	NA	NA	NA	DSP	Arm	c.916G>A	NA	
19	Male	13	At birth	LP	Upper and lower limbs	c.70 + 5G>A	NA	Lihi Atzmony et al[11]
20	Female	54	30	DSAP	Face, trunk, limbs	c.746T>C	NA	Li X et al[12]
21	Female	84	69	DSAP	Face, trunk, limbs	c.746T>C	NA	
22	Male	48	25	DSAP	Face, trunk, limbs	c.746T>C	NA	
23	Male	60	23	DSAP	Face, trunk, limbs	c.875A>G	NA	

Abbreviations: LP, Linear Porokeratosis, DSP, Disseminated Superficial Porokeratosis, DSAP, Disseminated Superficial Actinic Porokeratosis, PPPD, Porokeratosis Palmaris et Plantaris Disseminate, SCC, Squamous Cell Carcinoma.

The MVD gene occupies a pivotal position in the mevalonate pathway, a critical metabolic route in skin biology that regulates essential cellular processes such as growth, division, and differentiation.[13] Germline heterozygous mutations within this pathway have been implicated in both familial and sporadic forms of porokeratosis. Notably, patients with PK harboring MVD variants exhibited significant reductions in CD8 and γδT cells(Vγ9Vδ2T).[2] Given that γδT cells can secrete cytokines and chemokines, promoting the development of mixed-pattern immune-mediated inflammatory diseases, their depletion may have implications for disease pathogenesis.

The discovery that porokeratosis lesions arise from somatic recessive loss-of-function mutations in mevalonate pathway genes, such as MVD variants, holds promise for the development of innovative therapeutic strategies. The mevalonate pathway, therefore, emerges as a potential target for future porokeratosis therapies, offering hope for more effective management of this debilitating condition.

Consent Statement

The authors certify that the patient has given his informed consent for case details and images to be published. Institutional approval is required for this case study, and the approval was granted for this study to be published.

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Disclosure

The authors report no conflicts of interest in this work.

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