Dermoscopic Features and Gene Mutation in the Mevalonate Pathway of Five Sporadic Patients with Porokeratosis

Rui-Feng Sun, Hui Chen, Wei Zhu, Shi Lian

Department of Dermatology and Venereology, Xuanwu Hospital, Capital Medical University, Beijing 100053, China

Key words: Dermoscopy; Mutation; Porokeratosis

Porokeratosis (PK), first described in 1983, is a chronic parakeratotic skin disorder. Clinical types include porokeratosis of Mibelli (PM), disseminated superficial PK, disseminated superficial actinic porokeratosis (DSAP), facial PK, and ptychotropica porokeratosis (PP). Dermoscopic images of PK show an obvious annular margin with scales and an atrophied center.[1] Wood's lamp pictures of PK present a diamond necklace-like structure.[2] Gene mutations in mevalonate pathway enzymes, such as mevalonate kinase (*MVK*), phosphomevalonate kinase (*PMVK*), mevalonate decarboxylase (*MVD*), and farnesyl diphosphate synthase (*FDPS*), may be involved in the pathogenesis of PK.[3,4] In the present study, five sporadic patients with PK were recruited. Dermoscopic features were investigated, and genetic testing was conducted.

Sporadic patients with PK were diagnosed on the basis of typical clinical and histopathological features. PK is clinically characterized by a ring-like structure with an elevated border and atrophic center. Pathologically, PK is characterized by a parakeratotic column in the epidermis. The lesions selected for dermoscopic imaging were approximately 0.5 cm in diameter. The lesions were imaged under original magnification ×50 and then photographed under a dermoscope with white light. Venous blood was collected from all subjects to detect *MVK*, *PMVK*, *MVD*, and *FDPS* genes. Meanwhile, blood samples from 100 controls with normal phenotype were collected to rule out polymorphism. Genomic DNA was isolated from whole blood using a whole-blood genomic DNA extraction kit (Aidlab Inc., Beijing, China). *MVK*, *PMVK*, *MVD*, and *FDPS* sequences were obtained from the National Biological Information Center gene pool and University of California Santa Cruz database. Primers were designed through Primer Premier 5. Polymerase chain reaction (PCR) was performed in ABI GeneAmp 9700 PCR amplifier (Applied Biosystems, Foster, USA). PCR conditions are available upon request. All exons and flanking sequences of *MVK*, *PMVK*, *MVD*, and *FDPS* were sequenced on ABI PRISM 3730 automated sequencer (Applied Biosystems, Foster, USA). Bidirectional DNA sequencing was used to validate the detected gene mutations.

Among the five sporadic patients, two suffered from DSAP, two manifested facial PK, and one was diagnosed with PM. The male-to-female ratio was 2:3. The onset age ranged from 10 years old to 67 years old. Disease duration ranged from 3 years to 39 years. One patient suffered from light pruritus. Two patients presented with accompanying seborrheic keratosis. Many treatments, such as cryotherapy, retinoic acid ointment, and carbon dioxide laser treatment, exerted no significant effect on PK. The dermoscopic appearance of two patients with DSAP presented a brown ring-like structure with a raised border and scar-like center. Numerous scales were located on the border [Figure 1a]. The dermoscopic results for two patients with facial PK exhibited a black circular structure with a slightly raised border and atrophic center [Figure 1b]. The dermoscopic images from one patient with PM showed a brown annular structure with a ridged border and scar-like center [Figure 1c]. A novel *MVK* splicing mutation, designated as IVS4+1G>A (NM_000431.3), was detected in one patient with facial PK [Figure 1d].

The onset age of sporadic PK is in accordance with that reported in the literature.[3] PK is a chronic keratinization disorder with many different clinical types. DSAP and PM have generally been known by dermatologists. Facial PK, a rare variant, was

Address for correspondence: Dr. Shi Lian,
Department of Dermatology and Venereology, Xuanwu Hospital, Capital Medical University, Beijing 100053, China
E-Mail: drlianshi@sina.com

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.209905

Received: 16-03-2017 **Edited by:** Ning-Ning Wang
How to cite this article: Sun RF, Chen H, Zhu W, Lian S. Dermoscopic Features and Gene Mutation in the Mevalonate Pathway of Five Sporadic Patients with Porokeratosis. Chin Med J 2017;130:1747-8.

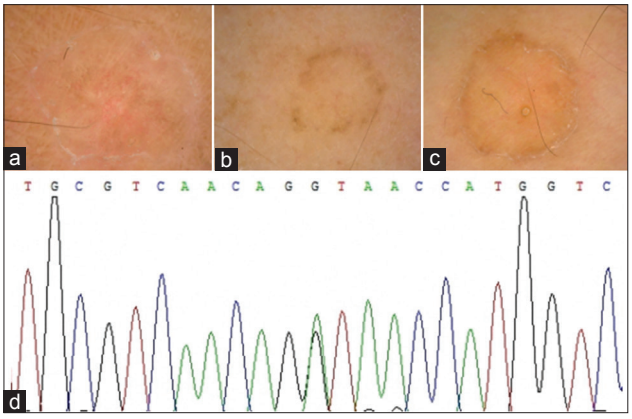

Figure 1: Dermoscopic features of disseminated superficial actinic porokeratosis viewed with white light (original magnification, ×50) (a); dermoscopic features of facial porokeratosis viewed with white light (original magnification, ×50) (b); dermoscopic features of porokeratosis of Mibelli viewed with white light (original magnification, ×50) (c); forward sequence diagram of mevalonate kinase gene splicing mutations in IVS4+1G>A (NM_000431.3) (d).

first documented in 1979. The cutaneous and histopathological characteristics of facial PK are similar to those of PK. Facial PK is different from others because the lesions are only localized on the face.[5] Some studies have shown that facial PK usually occurs in young women and may be associated with sun exposure. In the present study, two patients with facial PK are women. One has facial PK accompanied by seborrheic keratosis probably because exposure to sunlight may lead to facial PK and seborrheic keratosis. One patient experiences pruritus when she sweats. This occurrence may be because perspiration irritates PK lesions, thus causing itching. In the present study, cryotherapy, topical tretinoin, and carbon dioxide laser treatment exerted no effect on PK. Gutierrez *et al*.[5] reported that oral isotretinoin may be effective in the treatment of facial PK. However, this theory needs further research.

Dermoscopy is diagnostically valuable for PK patients.[1] In the present study, the dermoscopic image of DSAP is similar to those that have been previously documented. Moreover, the dermoscopic images of PM and facial PK are similar to that of DSAP. This result may be because of the similar lesions, genes, histopathological and immunohistochemical properties and changes in morphological characteristics of all PK types. However, few scales are attached to the edges of lesions in facial PK. The facial lesions of patients with DSAP also have few scales. The phenomenon is likely attributed to the use of facial cleanser and skincare products.[2]

Many mutations in *MVK*, *PMVK*, *MVD*, and *FDPS* genes have been detected in patients with PK. A total of 73% sporadic patients with PK had at least one mutation in four genes in the mevalonate pathway. This study only found a novel *MVK* splicing mutation, which was designated as IVS4+1G>A, in a sporadic patient with facial PK possibly because PK can be caused by other factors, such as sunlight exposure. The novel *MVK* gene mutation (IVS4+1G>A) may result in the absence of 52 amino acids (GPAEPGYRSVVGAAPRGGLGLQRRLLGVSGSSPP DCVRGDPKPAEGRGLRQQ) or two alpha helixes that are encoded by exon 4. The abnormal *MVK* structure caused by *MVK* gene mutations may negatively affect the mevalonate pathway. Finally, the growth of keratinocytes was abnormal and PK was caused. Zhang *et al*.[3] also discovered a novel *MVK* splicing mutation, which was designated as IVS4+2T>A, in a patient with PP.

In conclusion, dermoscopic characteristics of PK may not be correlated with clinical type but with lesion sites. However, this hypothesis deserves further study. A novel *MVK* splicing mutation (IVS4+1G>A) has expanded the database of *MVK* mutations and may help elucidate the pathogenesis of PK.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

This study was supported by a grant from the Beijing Natural Science Foundation (No. 7163216).

Conflicts of interest

There are no conflicts of interest.

References

1. Nicola A, Magliano J. Dermoscopy of disseminated superficial actinic porokeratosis. Actas Dermosifiliogr 2016. doi: 10.1016/j.ad.2015.09.025. [Epub ahead of print].
2. Sun R, Chen H, Zhu W, Lian S. Wood's lamp image of porokeratosis. Photodermatol Photoimmunol Photomed 2017;33:114-6. doi: 10.1111/phpp.12285.
3. Zhang Z, Li C, Wu F, Ma R, Luan J, Yang F, *et al.* Correction: Genomic variations of the mevalonate pathway in porokeratosis. Elife 2016;5:e14383. doi: 10.7554/eLife.14383.
4. Li M, Li Z, Wang J, Ni C, Sun Z, Wilson NJ, *et al.* Mutations in the mevalonate pathway genes in Chinese patients with porokeratosis. J Eur Acad Dermatol Venereol 2016;30:1512-7. doi: 10.1111/jdv. 13653.
5. Gutierrez EL, Galarza C, Ramos W, Tello M, De Paz PC, Bobbio L, *et al.* Facial porokeratosis: A series of six patients. Australas J Dermatol 2010;51:191-4. doi: 10.1111/j.1440-0960.2009.00616.x.