Coexist of Disseminated Superficial Actinic Porokeratosis and Porokeratosis Ptychotropica with A Novel MVK Gene Mutation: A Case Report and Literature Review

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Case report

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Abstract

Background: Porokeratosis is a rare, acquired or inherited disorder of keratinization. There are numerous clinical types of porokeratosis and they could coexist in one patient and in multiple members of an affected family. However, coexist of disseminated superficial actinic porokeratosis (DSAP) and porokeratosis ptychotropica (Ppt) is rare.

Case presentation: A 45-year-old man presented with long-standing skin lesions. Physical examinations found numerous small, brown 2- to 4-mm patches on his face and several hyperkeratotic, verrucous plaques on his trunk and extremities. His father and one of his brothers also had similar lesions for years. Skin biopsies showed a cornoid lamella in the epidermis. And we identified c.155 G>A mutation of the mevalonate kinase (MVK) gene converting a serine residue to asparagine (p.Ser52Asn) was the causative mutation for porokeratosis in this family. The clinicopathologic diagnosis of DSAP and Ppt with a novel MVK gene mutation was made. The hyperkeratotic plaques on the patient's scrotum were completely removed by microwave knife for more than 10 times.

Conclusion: We report an unusual case of DSAP coexisting with Ppt and identified a novel MVK gene mutation in this patient's family. The microwave knife is an effective and safe therapy for porokeratosis.

Background

Porokeratosis is a rare, acquired or inherited disorder of keratinization which presents as a keratotic papule or plaque with an annular ridge-like border[1]. Histologically, its characteristic is the cornoid lamella, a thin column of parakeratosis leading to the ridge-like hyperkeratotic border. Numerous types of porokeratosis have been described and there are reports of more than one type of porokeratosis developing in the same patient and in multiple members of an affected family[2–3]. Inherited or sporadic genetic defects play an important role in porokeratosis. The correlations between gene mutations and clinical phenotypes of porokeratosis were observed before[4]. Lesions of porokeratosis may influence patients' appearance or function. What's more, in some cases, development of squamouscell carcinoma within lesions of porokeratosis has been reported. However, therapeutic intervention with exact effect is lacking. In some patients, various topical, surgical, destructive, and systemic therapies appear to be effective now. Here we report a rare case of disseminated superficial actinic porokeratosis (DSAP) and porokeratosis ptychotropica (Ppt) associated with mevalonate kinase (MVK) gene mutation and successfully treated by surgical therapy.

Case Presentation

A 45-year-old man presented with long-standing skin lesions. The lesions started out as brown patches on his face and gradually spread to the trunk and extremities with verrucous plaques 30 years ago. The scrotum was involved 20 years ago.

Physical examinations found numerous small, brown 2- to 4-mm patches on his face (Fig. 1a) and several hyperkeratotic, verrucous plaques on his trunk and extremities (Fig. 1, b and c). The widespread verrucous plaques with erosions and crust on his scrotum (Fig. 1d) had already affected his normal life.

The patients reported no history of ultraviolet exposure, immunosuppression or immunodeficiency caused by HIV infection, tumors and drugs. However, his father and one of his brothers also had similar lesions for years.

Laboratory investigations including blood routine examination, hepatic and renal function, HIV antibody, treponema pallidumhemagglutination test, rapid plasma reagin test, human papillomavirus, hepatitis B and C, tumor markers and autoimmune screens were all negative.

Skin biopsies taken from the hyperkeratotic plaques of lesions on his scrotum showed irregular acanthosis and papillomatosis as well as a cornoid lamella in the epidermis and absence of the granular layer beneath it (Fig. 2).

After obtaining informed consent, genomic DNA was extracted from the proband, his affected and unaffected family members to amplify all exons of four mevalonate pathway genes including MVK, mevalonate decarboxylase (MVD), phosphomevalonate kinase (PMVK), and farnesyl diphosphate synthase (FDPS) with intronic flanking sequences using polymerase chain reaction. In addition, genomic DNA from 100 normal healthy Chinese individuals was extracted as controls. Bidirectional sequencing identified a heterozygous synonymous mutation c.155G > A in exon 18 of the MVK gene which could not be found in the unaffected family members and controls (Fig. 3). Thus, we identified c.155 G > A mutation of the MVK gene converting a serine residue to asparagine (p.Ser52Asn) was the causative mutation for porokeratosis in this family.

The clinicopathologic diagnosis of DSAP and Ppt with MVK gene mutation was made. The hyperkeratotic plaques on the patient's scrotum were completely removed by microwave knife for more than 10 times (Fig. 4). Luckily, the patient had no recurrence during 6-years follow-up.

Discussion

Porokeratosis represents a heterogeneous group of hereditary and acquired disorders of clonal hyperproliferation of keratinocytes[5]. The characteristic ridge-like, keratotic border called "cornoid lamella" confirms the diagnosis of porokeratosis. Several clinical variants of porokeratosis have been described, all of which share this distinctive feature.

DSAP is the most common type of porokeratosis. It presents as keratotic papules with a well-demarcated elevated border, usually ranging from 3 to 10 mm in diameter. They are typically skin-colored to tan–brown to pink–red in color. DSAP usually occurs in the third or fourth decade of life, and patients frequently report a history of extensive exposure to ultraviolet radiation. For this reason, it usually happened in sun-exposed areas, most commonly the shins and extensor forearms. Lesions on our patient face are the typical DSAP. Although 15% of DSAP patients have facial lesions, exclusively facial DSAP is an unusual clinical presentation[6]. Ppt is an unusual psoriasiform variant of porokeratosis[7–9]. This type of porokeratosis typically presents with pruritic, red to brown, keratotic, or verrucous papules and plaques on the buttocks or genital skin[9]. Sometimes, the lesions could coalesce. Due to clinical similarities, Ppt are often mistaken for psoriasis[10] and chronic eczema. In this case, skin biopsy is a useful measure to identify the diagnosis. For our patient, the verrucous plaques on his scrotum, buttocks and limbs were diagnosed as Ppt according to the pathologic findings.

There are reports of coexistence of multiple types of porokeratosis in the same individual[2, 11–20]. Co-occurrence of DSAP with Ppt is rare. To our knowledge, this is the fifth case in published English literature to date [8, 21–23](Table 1).

The pathogenesis of porokeratosis is poorly understood. Risk factors include genetic susceptibility, exposure to ultraviolet radiation, and immunosuppression. Some studies have found mutations in the phosphomevalonate kinase pathway genes, namely MVD, MVK, PMVK, and FDPS in patients with porokeratosis[24–25]. At least one mutation in the mevalonate pathway genes was reported to be found in up to 98 percent of the familial and over 70 percent of sporadic porokeratosis cases[4]. Among the above five patients, two had genetic results. Jia-Mei Peng et al identified a novel MVK missense mutation (c.1039G > C, p.Gly347Arg) in the family with coexisting DSAP and Ppt[23]. In our patient's family, another MVK missense mutation (c.155G > A, p.Ser52Asn) was found. Although this mutation was reported to be benign before, we suggest it is a novel mutation associated with porokeratosis. Functional analysis of this mutation *in vitro* and *in vivo* should be performed in further study. Based on the two cases, we imagine that the mutation of phosphomevalonate kinase pathway genes, especially MVK gene may play an important role in the pathogenesis of DSAP coexisting with Ppt.

Patients with porokeratosis has a 7.5–10% risk of malignant transformation to squamous cell carcinoma or basal cell carcinoma[26]. Thus, clinical surveillance with regular skin examinations and patient education about the warning signs of skin cancer and sun protection are necessary aspects of the management of all patients with porokeratosis. However, some patients with function impairments or appearance requirements want to eradicate the lesions of porokeratosis. The treatment of porokeratosis is various, but the disease is easy to recur. We chose microwave knife to remove the

hyperkeratotic plaques on patient's scrotum. The patient didn't have any function impairment caused by treatment and did not develop aggravation or recurrence during 6-years follow-up. This indicates that microwave knife is an effective and safe therapy for porokeratosis.

Conclusion

In conclusion, we report an unusual case of DSAP coexisting with Ppt and identified a novel MVK gene mutation in this patient's family. The microwave knife is an effective and safe therapy for porokeratosis and clinical surveillance for malignant transformation is necessary for all patients with porokeratosis

Abbreviations

DSAP: disseminated superficial actinic porokeratosis

Ppt: porokeratosis ptychotropica

MVK: mevalonate kinase

MVD: mevalonate decarboxylase

PMVK: phosphomevalonate kinase

FDPS: farnesyl diphosphate synthase

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee of Beijing Friendship Hospital. The patient provided written informed consent to have the case details and any accompanying images published. This study was conducted in accordance with the latest version of the Declaration of Helsinki. Each subject was ensured anonymity, which was maintained by using subject-specific numeric codes on all records, including registration cards.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Availability of data and materials

Please contact the author for data requests.

Competing interests

The authors declare that they have no competing interests.

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Author Contributions

HJX collected all the clinical data and wrote the draft. GDW completed the gene analysis. LFL revised the manuscript. All authors read and approved the final manuscript.

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Table

Table 1
Clinical features of patients with coexisting DSAP and Ppt

Case	Gender	Age	Ethnicity	Nationality	Clinical Variants	Genetics	Risk factors	Treatment
C. Thomas et al ²¹	Female	78yr	NA	United Kingdom	DSAP, Ppt	NA	None	NA
Kelly McGuigan et al ⁸	Male	84yr	NA	United States	DSAP, Ppt	NA	Sun exposure, nonmelanoma skin cancer	0.025% tretinoin cream, 0.05% tazarotene cream.
Jenny Murase et al ²²	Female	73yr	Korean	Korea	DSAP, Ppt, linear porokeratosis	NA	Family history	NA
Jia-Mei Peng et al ²³	Male	70yr	Chinese	China	DSAP, Ppt	MVK missense mutation (c.1039G > C, p.Gly347Arg)	Family history	oral acitretin (20 mg daily)
Our patient	Male	45yr	Chinese	China	DSAP, Ppt	MVK missense mutation (c.155G > A, p.Ser52Asn)	Family history	microwave knife

Figures

Figure 1

Skin lesions of the patient. a: Small, brown patches on face. b, c, d: hyperkeratotic, verrucous plaques on trunk and extremities and widespread verrucous plaques with erosions and crust on scrotum.

Figure 2

Histopathological examination showed a cornoid lamella in the epidermis (hematoxylin–eosin, original magnifications: $\times 100$).

Figure 3

Analysis of the mutation in the MVK gene. A novel MVK missense mutation (c.155G>A) in the family.

Figure 4

The lesions on the patient's scrotum were completely removed after microwave knife treatment.

Supplementary Files

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