

70331_Auto_Edited-LJH.docx

Name of Journal: *World Journal of Clinical Cases*

Manuscript NO: 70331

Manuscript Type: CASE REPORT

Mixed porokeratosis with a novel mevalonate kinase gene mutation: A case report

Hong-Jun Xu, Guang-Dong Wen

Abstract

BACKGROUND

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

CASE SUMMARY

A 45-year-old man presented with long-standing skin lesions. Physical examination identified numerous small, brown 2-mm 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 indicated a cornoid lamella in the epidermis. We identified c.155G>A mutation in the mevalonate kinase (MVK) gene, which converted a serine residue to asparagine (p.Ser52Asn) and was causative for porokeratosis in this family. A 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 more than 10 times by a microwave knife.

CONCLUSION

An unusual case of DSAP coexisting with Ppt harbored a novel MVK gene mutation also present in the patient's family.

INTRODUCTION

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]. Its main histological characteristic is a cornoid lamella, a thin column of parakeratosis leading to a ridge-like hyperkeratotic border. Numerous types of porokeratosis have been described and ³ there are reports of more than one type of porokeratosis developing in the same patient and in multiple members of an affected family^[2]. Inherited or sporadic genetic defects have an important role in porokeratosis. Correlations between gene mutations and clinical phenotypes of porokeratosis have been reported previously^[3]. Porokeratosis lesions may alter a patient's appearance or function. Furthermore, some cases develop squamous cell carcinoma within the porokeratosis lesions. Currently, no therapeutic interventions with good efficacy are available although various topical, surgical, destructive, and systemic therapies appear to be effective in some patients. Here, we report a rare case of disseminated superficial actinic porokeratosis (DSAP) and porokeratosis ptychotropica (Ppt) associated with a mevalonate kinase (MVK) gene mutation and successfully treated by surgical therapy.

CASE PRESENTATION

Chief complaints

A 45-year-old man complained of long-standing skin lesions.

History of present illness

The lesions started as brown patches on his face and gradually spread to the trunk and extremities with verrucous plaques 30 years ago. The scrotum became involved 20 years ago.

History of past illness

The patient had no medical history and reported no history of ultraviolet exposure, immunosuppression, or immunodeficiency caused by human immunodeficiency virus (HIV) infection, tumors, or drugs.

Personal and family history

The patient's father and one of his brothers had similar lesions for years.

Physical examination

Physical examinations identified numerous small, brown 2-mm to 4-mm patches on his face (Figure 1A) and several hyperkeratotic, verrucous plaques on his trunk (Figure 1B) and extremities (Figure 1C). The widespread verrucous plaques with erosions and crust on his scrotum (Figure 1D) affected his normal life.

Laboratory examinations

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

Imaging examinations

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 the absence of the granular layer beneath it (Figure 2).

Gene test

After obtaining informed consent, genomic DNA was extracted from the proband and his affected and unaffected family members, and all exons of four mevalonate pathway genes including MVK, mevalonate decarboxylase (MVD), phosphomevalonate kinase (PMVK), and farnesyl diphosphate synthase (FDPS) with intronic flanking sequences

4
were amplified by PCR. 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 was not present in the unaffected family members and controls (Figure 3). This c.155 G>A mutation in the MVK gene converted a serine residue to asparagine (p.Ser52Asn) and was the causative mutation for porokeratosis in this family.

FINAL DIAGNOSIS

A clinicopathologic diagnosis of DSAP and Ppt with MVK gene mutation was made.

TREATMENT

The hyperkeratotic plaques on the patient's scrotum were completely removed more than 10 times by a microwave knife (Figure 4).

OUTCOME AND FOLLOW-UP

The patient has had no recurrence during 6-years of follow-up.

DISCUSSION

2
Porokeratosis represents a heterogeneous group of hereditary and acquired disorders of the clonal hyperproliferation of keratinocytes^[4]. The characteristic ridge-like, keratotic border termed the "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 mm 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 occurs in body areas exposed to the sun, especially the shins and extensor forearms. Lesions on

our patient's face were typical of DSAP. Although 15% of DSAP patients have facial lesions, exclusively facial DSAP is an unusual clinical presentation^[5]. Ppt is an unusual psoriasiform variant of porokeratosis^[6-8], which typically presents with pruritic, red to brown, keratotic, or verrucous papules and plaques on the buttocks or genital skin^[8]. Sometimes, these lesions can coalesce. Because of their clinical similarities, Ppt is often mistaken for psoriasis^[9] and chronic eczema. Therefore, a skin biopsy is a useful method for differential diagnosis. The verrucous plaques on our patient's scrotum, buttocks, and limbs were diagnosed as Ppt according to the pathologic findings.

Previous studies have reported the coexistence of multiple types of porokeratosis in the same individual^[10-20]; however, the co-occurrence of DSAP with Ppt is rare. To the best of our knowledge, this is the fifth case reported in the English literature to date^[7,21-23](Table 1).

The pathogenesis of porokeratosis is poorly understood. Risk factors include genetic susceptibility, exposure to ultraviolet radiation, and immunosuppression. Previous studies reported mutations in the phosphomevalonate kinase pathway genes, including MVD, MVK, PMVK, and FDPS in patients with porokeratosis^[24,25]. At least one mutation in a mevalonate pathway gene was found in 98% of familial cases and > 70% of sporadic porokeratosis cases^[3]. Among the above five patients previously reported, two had genetic results. Peng *et al*^[23] identified a novel MVK missense mutation (c.1039G>C, p.Gly347Arg) in a family with coexisting DSAP and Ppt. In our patient's family, another MVK missense mutation (c.155G>A, p.Ser52Asn) was found. Although this mutation was previously reported as benign, we suggest it is a novel mutation associated with porokeratosis. Functional analysis of this mutation *in vitro* and *in vivo* should be performed in future studies. The findings of our two cases suggest the mutation of phosphomevalonate kinase pathway genes, especially the MVK gene, might have an important role in the pathogenesis of DSAP coexisting with Ppt. Genetic analysis is useful in affected families to predict the occurrence of these lesions in other individuals of the same family.

Patients with porokeratosis have 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 for all patients with porokeratosis. However, some patients with functional impairments or appearance requirements want to have their porokeratosis lesions removed. There are five main types of treatment for porokeratosis: Topical or systemic drug therapy, surgical excision, cryotherapy, laser ablation, and photodynamic therapy. However, the disease commonly reoccurs. We used a microwave knife to remove the hyperkeratotic plaques on the patient's scrotum. The patient did not show any functional impairment related to this treatment and did not develop disease aggravation or recurrence during 6-years of follow-up. This indicates that the 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.

8%

SIMILARITY INDEX

PRIMARY SOURCES

1 Jia - Mei Peng, Xue - Min Xiao, Jia - Wen Chen, Li - Fen Chen, Bo Cheng, Ming - Kai Ji, Zheng - Hua Zhang. " Novel mutation in gene for co - occurrence of disseminated superficial actinic porokeratosis with porokeratosis ptychotropica ", The Journal of Dermatology, 2021 62 words — 4%

[Crossref](#)

2 Johann de Wet, Minette Swart, H. Francois Jordaan, Johann W. Schneider, Suzanne Mulder, Willem I. Visser. "An unusual case of generalized hyperkeratotic and verrucous porokeratosis", JAAD Case Reports, 2020 15 words — 1%

[Crossref](#)

3 M Nessa, L Khondker, MA Bari, MSI Khan, M Rahman, SY Moni. "Porokeratosis with an Invasive Squamous Cell Carcinoma: A Case Report and Review of Literature", Journal of Bangladesh College of Physicians and Surgeons, 2014 15 words — 1%

[Crossref](#)

4 C.-R. Li, M.-J. Jiang, D.-B. Shen, H.-X. Xu, H.-S. Wang, X. Yao, Y. Zhang, W.-Q. Zhou, B. Wang. "Two novel mutations of the nicastrin gene in Chinese patients with acne inversa", British Journal of Dermatology, 2011 13 words — 1%

[Crossref](#)

5 www.statpearls.com

EXCLUDE QUOTES ON
EXCLUDE BIBLIOGRAPHY ON

EXCLUDE MATCHES OFF