LETTER TO THE EDITOR

A novel non-frameshift deletion in MVK gene responsible for disseminated superficial actinic porokeratosis in one Chinese family

Dear Editor,

Disseminated superficial actinic porokeratosis (DSAP), a genodermatosis transmitted as an autosomal dominant trait featuring disorder of keratinization, is characterized clinically by annular plaques with an atrophic centre and hyperkeratotic edges.1–4 Recently, Zhang et al.2 reported MVK mutations in 33% familial and 16% sporadic patients with DSAP by exome sequencing. Here, we report a single novel mutation of MVK, p.Cys161_Arg176del, in a Chinese family suffering from DSAP.

A four-generation family with two affected individuals was recruited in this study (Fig. 1a). The proband was 58-year-old male farmer (II1) presented with multiple lesions on the face, trunk and extremities for 10 years. His mother, daughter and grandsons did not show any DSAP-related abnormality. His son, a 33-year-old male farmer (III3), had a similar condition for 2 years. He was overexposed to sunlight as he spent most of his time outdoors. His father (I1) had similar DSAP abnormality at the onset age of 40. Cutaneous examination on the face, trunk and extremities showed multiple disseminated distributed round to ovoid pigmented papules and plaques measuring approximately 0.5–2 cm in diameter with an atrophic and desquamative centre and slightly elevated borders (Fig. 1b,c). Histopathological examination of the pigmented lesion showed an atrophic epidermis with the presence of rare cornoid lamellae presenting as thin columns of parakeratin over a focal invagination of epidermis with loss of granular layer and apoptotic keratinocytes (Fig. 1d). After ethical approval was granted, written informed consent was obtained from the participants, in compliance with the Declaration of Helsinki.

Genomic DNA was isolated from peripheral blood of the patients, unaffected family members and 100 unrelated healthy individuals using a Qiagen kit (Hilden, Germany). All coding exons of the MVK gene together with boundary exon–intron sequences were amplified using published primers.2 Direct sequencing of all coding and exon–intron boundary sequences identified a novel heterozygous non-frameshift deletion in exon 5 of the MVK gene, designated as c.480_527del48 in the proband, his son (III3) and his grandson (IV4) (Fig. 2a). This mutation has not been reported in literatures or recorded in mutation databases. Other unaffected individuals (II2, III1, III2,

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Figure 1 Pedigree, clinical phenotype and mutation information of the family. (a) Genealogical tree of the with DSAP. Clear and filled symbols represent unaffected and affected individuals, respectively. A dotted circle indicates a carrier. (b, c) Typical lesions with round to ovoid pigmented papules and plaques with slightly elevated borders on the forearm and leg detected in the proband with DSAP. (d) A biopsy of the proband revealed a typical cornoid lamella in the epidermis. Histopathological examination showed an atrophic epidermis with the presence of rare cornoid lamellae presenting as thin columns of parakeratin over a focal invagination of epidermis with loss of granular layer and apoptotic keratinocytes. [haematoxylin and eosin (H&E) staining x100 magnification].

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Figure 2 Mutation analysis of MVK. (a) Identification of the heterozygous mutation c.480_527del48 (p.Cys161_Arg176del) in the MVK gene by direct sequencing (reverse strand) in two cases and one carrier. (b) The sequencing result of exon 5 from control.
III4, IV1, IV2, IV3 and IV5) in the family and unrelated controls did not show this change (Fig. 2b).

The proband and his son within this study are farmers and spend most of the day outdoors. They had multiple round to ovoid pigmented papules and plaques on the face, trunk and extremities. Histopathological examination showed a typical cornoid lamella in the epidermis. Clinical and histological features supported the diagnosis of DASP.

MVK locates on 12q24, has four conserved regions that are predicted as functional domains and encodes the peroxisomal enzyme mevalonate kinase, which is involved in the biosynthesis of cholesterol and isoprenoid.5–7 Cholesterol plays an important role in the skin barrier function.8 In our study, we identified MVK(p.Cys161_Arg176del) mutation in two cases with DSAP in this family. Further genetic tests on the other family members found the same mutation in one of the proband’s grandson (IV4), who is currently 4 years old but does not show any DSAP-related abnormality. The proband, his farther (I1) and his son (II1) had late-onset DSAP at the age of 48, 40 and 31, respectively, which indicated that heterozygous deletion (p.Cys161_Arg176del) in the second conserved region in MVK gene might be related to the later age of onset. To the best of our knowledge, 44 MVK mutations were identified in Chinese familial or sporadic patients with DSAP.8 This study extends the mutation spectrum of MVK.

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