Dyskeratosis Congenita with DKC1 Mutation: A Case Report

Xing-Yun Zhao1,2*, Wei-Long Zhong3*, Jie Zhang1, Gang Ma1, Hao Hu2, Bo Yu1,2

From the 1Department of Dermatology, Peking University Shenzhen Hospital, Shenzhen, 2Shenzhen Key Laboratory for Translational Medicine of Dermatology, Shenzhen, 3Department of Dermatology, Peking University First Hospital, Beijing, China.
E-mail: yubomd@163.com

*These authors contributed equally to this work.

Indian J Dermatol 2020:65(5):426-7

Sir,

Dyskeratosis congenita (DC) is a rare inherited disease characterized by mucocutaneous triad (reticular skin pigmentation, nail dystrophy, and oral leukoplakia), bone marrow failure, and cancer susceptibility.[1,2] To date, 12 genes involved in telomere length maintenance have been reported to be associated with DC.[3] DKC1 was identified as the causative gene for DC with an X-linked pattern of inheritance.[3] Here, we present a recurrent DKC1 mutation in a Chinese DC family.

A nonconsanguineous Chinese family with X-linked recessive DC was referred to our department [Figure 1a]. The proband was a 24-year-old male who developed reticulate hyperpigmented and hypopigmented macules on the neck at 12 year of age [Figure 1b]. These macules gradually spread to the face, extremities, and trunk. Two years later, fragile nails in all fingers and toes were noted [Figure 1c]. At the age of 18, blisters and erosions, followed by white spots, appeared on the oral mucosa and tongue [Figure 1d]. He was otherwise healthy. Two other affected brothers showed similar progression. His younger brother showed additional thrombocytopenia, and the other brother had surgical removal of his oral leukoplakia at 20 year of age as the leukoplakia had progressed to squamous cell carcinoma [Figure 1e]. A skin biopsy from hypopigmented macules on the upper chest of the proband showed marked thinning and flattening of the epidermis and melanophages in the upper dermis [Figure 1f].

Sanger sequencing targeting DKC1 was performed after informed consent was obtained and revealed a recurrent hemizygous c. 1226C > G (p.P409R) mutation in exon 12 in the proband. The mutation segregated perfectly with the phenotypes in this family and was predicted to be damaged in silico.

The proband showed typical mucocutaneous manifestations and had a recurrent P409R mutation in DKC1, which led to the diagnosis of DC. Previously, one case with the same mutation reported that some female carriers also manifested features of DC due to X-chromosome skewing.[4] These phenotypic invariances may be due to unknown environmental or other genetic factors.

DKC1 encodes dyskerin, which is the nucleolar protein associated with small nucleolar RNAs (snoRNPs) in H/ACA snoRNP complexes.[2,5] Most mutations were single base substitutions, which were mainly located in exons 3, 4, 10, 11, and 12 [Figure 2]. Exons 3, 4, and 5 encode the DKCLD domain, in which mutations...
may affect domain–domain interactions. The other mutations were clustered in exons 10, 11, and 12, which encoded the telomerase RNA binding and the pseudouridine synthase domain. [2,5] These mutations caused defects in pseudouridylation and ribosome biogenesis, which led to the consequent phenotype of DC.

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 work was supported by the National Natural Science Foundation of China (grant no. 81673053), the fund of “San-ming” Project of Medicine in Shenzhen (no. SZSM201812059) and Shenzhen Research Grants (JCYJ20160428173958860, JCYJ20170411090739316, JCYJ20170306161807726).

Conflicts of interest

There are no conflicts of interest.

References

1. Fernandez GMS, Teruya-Feldstein J. The diagnosis and treatment of dyskeratosis congenita: A review. J Blood Med 2014;5:157-67.
2. Mason PJ, Bessler M. The genetics of dyskeratosis congenita. Cancer Genet 2011;204:635-45.
3. Ratnasamy V, Navaneethakrishnan S, Sirisena ND, Grüning NM, Brandau O, Thirunavukarasu K, et al. Dyskeratosis congenita with a novel genetic variant in the DKC1 gene: A case report. BMC Med Genet 2018;19:85.
4. Alder JK, Parry EM, Yegnasubramanian S, Wagner CL, Lieblich LM, Auerbach R, et al. Telomere phenotypes in females with heterozygous mutations in the dyskeratosis congenita 1 (DKC1) gene. Hum Mutat 2013;34:1481-5.
5. Cerrudo CS, Mengual Gómez DL, Gómez DE, Ghiringhelli PD. Novel insights into the evolution and structural characterization of dyskerin using comprehensive bioinformatics analysis. J Proteome Res 2015;14:874-87.

How to cite this article: Zhao XY, Zhong WL, Zhang J, Ma G, Hu H, Yu B. Dyskeratosis congenita with DKC1 mutation: A case report. Indian J Dermatol 2020;65:426-7.

Received: December, 2018. Accepted: December, 2018.