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CORRESPONDENCE

A novel mutation of the RNA-specific adenosine deaminase 1 gene in a Taiwanese patient with dyschromatosis symmetrica hereditaria and Becker's nevus-like lesion

Dear Editor,

Dyschromatosis symmetrica hereditaria (DSH, Online Mendelian Inheritance in Man 127400) is a rare autosomal dominant pigmentary disorder characterized by intermingled hyper- and hypopigmented macules on the face and the dorsal aspects of the extremities with onset during infancy or early childhood.[1] DSH had been reported primarily in Japan, Taiwan, and China.[2] Mutations in the RNA-specific adenosine deaminase 1 (*ADAR1*) gene are known to be responsible for the disorder. To date, more than 120 mutations in the *ADAR1* gene associated with the disorder have been reported.[3] Here we report a novel mutation of *ADAR1* c.1944C>G (p.Y648X) in a Taiwanese patient with DSH and a Becker's nevus-like lesion on the buttock.

A 13-year-old male patient presented to our clinic with reticulate hyper- and hypopigmented macules on the dorsal aspect of the hands progressively for 4 years (Figure 1A). Mild lesions with off-white macules on the dorsal feet were also noted. There were also some freckle-like macules scattered on the face and neck. In addition, one brown hairy pigmented plaque on the left buttock, which occurred gradually at age 10 years, was noted during examination. The clinical features suggested a Becker's nevus-like lesion (Figure 1B), however, the diagnosis was not confirmed by histopathology. There was no family history of DSH.

Genomic DNA was extracted from the whole blood samples of the patient and his parents with informed consent. All exons of the *ADAR1* gene, including intron–exon boundaries, were amplified using polymerase chain reaction. A novel nonsense mutation c.1944C>G (p.Y648X) in exon 5 of the *ADAR1* gene was identified (Figure 2).

ADAR1, also called *DSRAD* (double-stranded RNA specific adenosine deaminase), spans 26,191 bp of genomic sequence on chromosome 1q21.3, and contains 15 exons. ADAR1 is a modular protein with a C-terminal deaminase catalytic domain, three centrally located dsRNA-binding domains (dsRBDs) and one or two N-terminal Z-DNA–binding domains.[4] The *ADAR1* mutation (p.Y648X) in exon 5 identified in the present case leads to a premature termination codon with incomplete dsRNA-binding motif and loss of adenosine deaminase domain. Previous studies indicate that both the deaminase domain and the dsRNA-binding domain are important for exerting ADAR1 catalytic activity.[3]

Becker's nevus is an organoid nevus characterized by hyperpigmentation, increased hairiness, and hamartomatous augmentation of smooth muscle fibers.[5] The typical location of Becker's nevus is the upper trunk, shoulder, and upper arms, however, in the present case the Becker's nevus-like lesion was located on the buttock. To our knowledge, there is no report on the coexistence of DSH and Becker's nevus and no association between Becker's nevus and mutations in the *ADAR1* gene. The coexistence of Becker's nevus-like lesion and the other developmental abnormality of the skin in this patient raised the concern of Becker's nevus syndrome. However, the absence of Becker's nevus

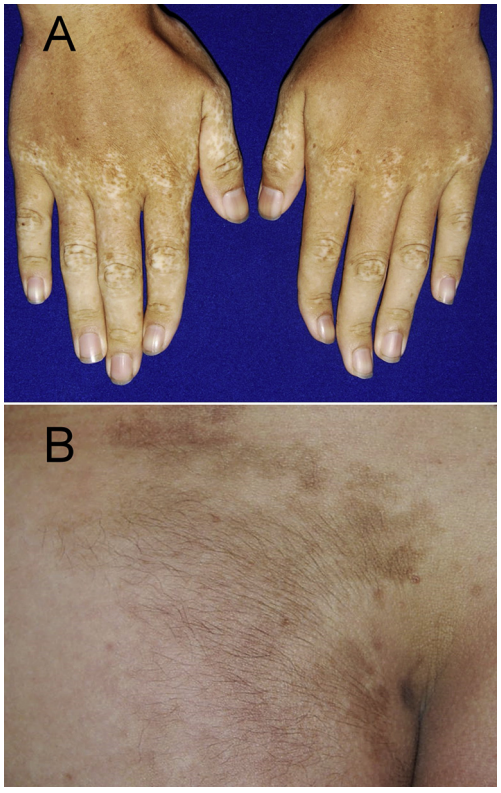

Figure 1 Clinical presentations of dyschromatosis symmetrica hereditaria and Becker's nevus-like lesion. (A) Mixed hyper- and hypopigmented macules on the dorsal aspect of the hands. (B) One brown hairy plaque on the left buttock.

Conflicts of interest: The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in this article.

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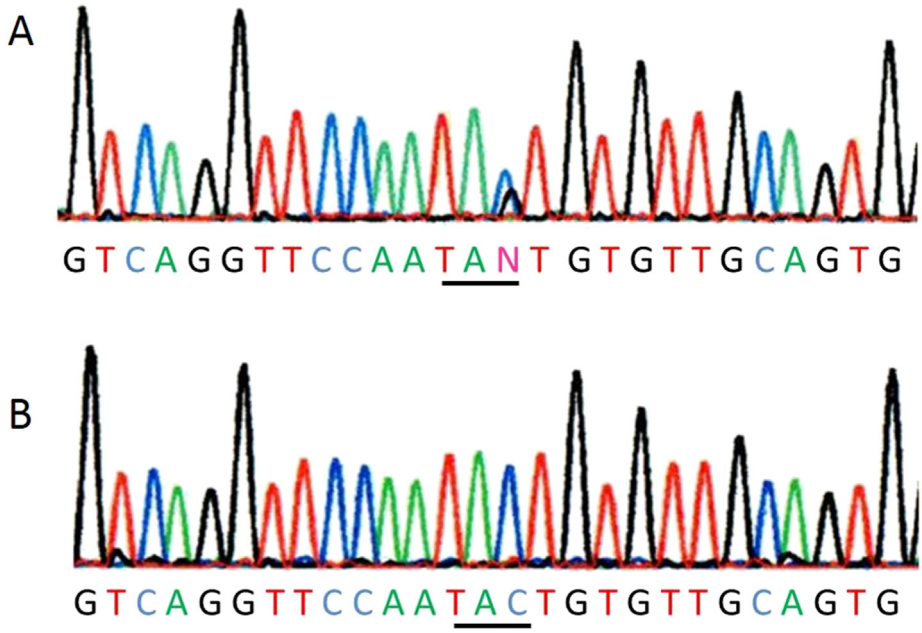

Figure 2 Mutational analysis revealed: (A) a nonsense mutation (p.Y648X) in exon 5 of *ADAR1* gene compared with (B) the control gene from the parent.

syndrome-associated developmental abnormalities, including ipsilateral hypoplasia of breast and skeletal anomalies including scoliosis, spina bifida occulta, or ipsilateral hypoplasia of a limb, as proposed by Happle and Koopman[5] in 1997, did not support this diagnosis. In conclusion, by reporting this peculiar coexistence of DSH and Becker's nevus-like lesion and a novel mutation in *ADAR1* gene, we would like to expand the clinical and genetic spectrum of DSH.

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