GENETICS AND GENODERMATOSES

DYSKERATOSIS CONGENITA: A MULTIDISCIPLINARY APPROACH.

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Background: Dyskeratosis congenita (DC) is an inherited bone marrow failure syndrome caused by germline mutations in telomere genes. It can be inherited in an X-linked, autosomal recessive or dominant pattern. In its classic form, it is characterized by mucocutaneous abnormalities, bone marrow (BM) failure, and a predisposition to cancer. Typical clinical features consist of oral leukoplakia, reticular skin pigmentation, and nail dystrophy. Hoyeraal-Hreidarsson syndrome (HHS) is a rare, severe variant of DC, and is characterized by growth retardation of prenatal onset, microcephaly, cerebellar hypoplasia, BM failure, and early mortality.

Observation: A 4-year-old male patient, delivered preterm (35+6 weeks), the product of consanguineous parents, with a history of thrombocytopenia from several months of age. He also had neurological developmental delay and failure to thrive. Physical examination revealed microcephaly, short stature, leukoplakia on the tongue, extensive caries, and loss of dental pieces. No reticular skin pigmentation or nail dystrophy was observed. A brain magnetic resonance imaging scan showed atrophy of the cerebellum.
The karyotype was normal 46 XY. No mutations were detected for Fanconi anemia, Diamond–Blackfan anemia, Shwachman-Diamond syndrome, or inherited thrombocytopenia in peripheral blood. A genetic test revealed a homozygous missense mutation (c.296T>G) in RTEL1. With these clinical, genetic, and radiologic findings, the diagnosis of Hoyeraal-Hreidarsson syndrome was proposed.

Key message: Management of DC requires a multidisciplinary approach. This case illustrates the value of clinical, supplementary evaluations of patients with DC in order to identify less frequent variants as HHS. It is not uncommon for BM failure to present before the typical mucocutaneous features, and this is able to be recognized due to the advances in genetics. Early recognition and appropriate genetic counseling, follow-up, and treatment are crucial because of the high mortality of this disorder.