GENETICS AND GENODERMATOSES

LINEAR AND WHORLED NEVOID HYPERMELANOSIS ASSOCIATED WITH A NOVEL KITLG SOMATIC MUTATION

A Yuki [1] - S Shinkuma [1] - R Yokoyama [1] - T Kawai [1] - Y Kabata [1] - R Hayashi [1] - H Nguyen [1] - K Takamura [2] - K Tomiyama [3] - R Abe [1]

Niigata University, Division Of Dermatology, Niigata, Japan [1] - Niigata University, Division Of Molecular And Diagnostic Pathology, Niigata, Japan [2] - Niigata City General Hospital, Department Of Dermatology, Niigata, Japan [3]

Background: Linear and whorled nevoid hypermelanosis (LWNH) is characterized by hyperpigmentation following Blaschko's line. Most recently, a postzygotic mutation in KITLG was identified only on affected skin of an LWNH patient. KIT-ligand (KITLG), known as stem cell factor, is a ligand for the tyrosine kinase c-KIT receptor that acts exclusively in a melanocyte-autonomous manner. In this report, we show a patient with LWNH who has a novel KITLG mutation in the epidermis of hyperpigmented lesion.

Observation: An 11-year-old Japanese boy presented with diffuse hyperpigmentation since 4 months of age. Physical examination revealed diffuse swirls and streaks of macular hyperpigmentation following the lines of Blaschko on the whole body. Histological examination of the hyperpigmented skin showed an increased number of melanocytes and hyperpigmentation in the lower epidermis compared with unaffected skin. Immunohistochemical stains using anti-KITLG antibody revealed cytoplasmic staining of the lower epidermis. C-KIT staining showed increased epidermal expression in basal keratinocytes. S-100, HMB45, and Melan A staining confirmed an increased number of melanocytes. Transmission electron microscopy revealed an increased melanocyte population, dendrite extension into the spinous layer, and increased melanosomes within keratinocytes. A novel heterozygous missense mutation, c.325G>A (Asp109Asn), was detected only in the epidermis of hyperpigmented lesion by direct sequencing analysis of KITLG. The missense mutation was not identified in the dermis of hyperpigmented lesion, the dermis and epidermis of normal skin and peripheral blood mononuclear cells. The Asp109 located in extracellular domain of KITLG is highly conserved amino acid residue among diverse species.

Key message: We report here an LWNH patient with a novel heterozygous missense mutation, c.325G>A (Asp109Asn) in KITLG only in the epidermis of hyperpigmented lesion. Currently, we are in the process of additional analysis on how KITLG affects melanogenesis in LWNH.