GENETICS AND GENODERMATOSES

EXPANDING THE GENOTYPE-PHENOTYPE CORRELATIONS OF KERATINOPATHIC ICHTHYOSIS: A CASE SERIES

Zhou Yang [(1)] - Zhe Xu [(1)] - Lin Ma [(1)]

Beijing Children's Hospital, Capital Medical University, National Center For Children's Health, China, Department Of Dermatology, Beijing, China [(1)]

Background: Keratinopathic ichthyosis (KPI) represent a group of mostly autosomal dominant disorders result from mutations in keratin 1(KRT1), keratin 2 (KRT2) or keratin 10 (KRT10). Mutations in KRT1 or KRT10 underlie epidermolytic ichthyosis (EI), ichthyosis with confetti (IWC), ichthyosis Curth-Macklin (ICM), annular, autosomal recessive and naevoid variants, whereas mutations in KRT2 lead to superficial EI. Genotype-phenotype correlations in KI remain complex.

Observation: Ten KPI patients (seven EI, two ICM and one superficial EI) were studied. Ten heterozygous mutations (including five novel mutations) were found in KRT1, KRT2 or KRT10. In EI, there were three recurrent mutations (p. Arg154His, p. Arg156His, p. Leu453Pro) and two novel mutations (p. Met150Val, p. Ile446fs) in KRT10, while a recurrent mutation (p. Leu187Phe) and a novel mutation (p. Gly533Metfs*82) in KRT1. Mutations in KRT1 lead to severe palmoplantar hyperkeratosis (PPK), while p. Ile446fs in KRT10 also developed severe PPK. Gly533Metfs*82 in KRT1 developed localized mild ichthyosis at elbow and knee with PPK. Novel mutations p. Met150Val and p. Ile446fs in KRT10 had generalized erythoderma without blistering. Although frameshift mutations affecting tail domains of KRT1 or KRT10 related to IWC, we found a novel frameshift mutation (p. Gly622Cysfs) in tail domains of KRT1 and a novel missense mutation (p. Leu436Pro) in exon 6 of KRT10 both caused ICM. Gly622Cysfs in KRT1 presented with generalized hystrix-like hyperkeratosis and palmoplantar involvement. Leu436Pro in KRT10 presented with relatively milder hyperkeratosis but extensive hyperpigmentation.

Key message: This study adds new data to genotype-phenotype correlations of KI. Different from previously reports, mutation (p. Ile446fs) in KRT10 developed severe PPK; mutation (p. Gly533Metfs*82) in KRT1 developed localized phenotype and PPK; mutations in KRT10 could have generalized erythoderma without blistering; frameshift mutation (p. Gly622Cysfs) in tail domains of KRT1 and missense mutation (p. Leu436Pro) in exon 6 of KRT10 could both cause ICM.