EPIDEMIOLOGY

MC1R VARIANTS IN CHILDHOOD AND ADOLESCENT MELANOMA: A POOLED-ANALYSIS FROM A LARGE WORLDWIDE MULTICENTER COHORT OF PATIENTS

C Pellegrini [(1)] - F Botta [(2)] - D Massi [(3)] - C Martorelli [(1)] - F Facchetti [(4)] - S Gandini [(5)] - Mc Fargnoli [(1)] - S Raimondi [(6)]

University Of L'aquila, Department Of Dermatology, Department Of Biotechnological And Applied Clinical Sciences, L'aquila, Italy [(1)] - Università Degli Studi Di Milano-bicocca, Department Of Statistics And Quantitative Methods, Milan, Italy [(2)] - University Of Florence, Division Of Pathological Anatomy, Department Of Surgery And Translational Medicine, Florence, Italy [(3)] - University Of Brescia, Spedali Civili Brescia, Pathology Section, Department Of Molecular And Translational Medicine, Brescia, Italy [(4)] - Istituto Europeo Di Oncologia, Molecular And Pharmaco-epidemiology Unit, Milan, Italy [(5)] - Istituto Europeo Di Oncologia, Division Of Epidemiology And Biostatistics, Milan, Italy [(6)]

Introduction: Cutaneous melanoma (CM) is rare in children, representing 1-3% of all paediatric malignancies. It distinct clinico-pathological characteristics from adult CM, suggesting that different factors contribute to its development. MC1R is a key gene for skin pigmentation, is highly polymorphic and MC1R gene variants are associated with CM in different populations, and with congenital melanocytic naevi in children.

Objective: To evaluate the impact of MC1R gene variants on childhood/adolescent CM susceptibility in a large case-case study comparing the prevalence of MC1R variants between childhood/adolescent and adult CM patients.

Materials and Methods: Data of 233 paediatric (age ≤20 years) and 466 geographically matched adult (age ≥35 years) CM patients were gathered through the M-SKIP Project and other European centers. We calculated the odds ratio (OR) for MC1R variants by multivariable logistic regression. Subgroup analysis was done for children aged ≤18 and ≤14, and by population ancestry.

Results: Children/adolescents had a higher probability of carrying MC1R r variants than adults (OR: 1.96; 95%CI: 1.23-3.13). In stratified analysis, ORs for r alleles were higher in populations with Southern European ancestry (OR: 1.89; 95%CI: 1.10-3.23) and in children ≤14 years (OR: 3.89; 95%CI: 1.12-13.47). Most of the investigated variants were observed with higher frequency in paediatric CM compared to adult CM, with significant results obtained for V60L (OR: 1.76; 95%CI: 1.10-2.81) variant.

Conclusions: Based on our pooled-analysis of the largest worldwide multicenter cohort of paediatric patients with MC1R genetic data, we found that MC1R r variants played a major role in paediatric CM compared to adult CM, especially in children ≤14 years and in patients of Southern European ancestry. Our study represents the first step to comprehend the genetic background of childhood/adolescent CM and to elucidate the diversity of paediatric and adult CM, with potential clinical impact.