O203

2-hour Oral Session

Association between polymorphism in the gene encoding monocyte chemoattractant protein 1 and sensorineural hearing loss in congenital cytomegalovirus infection

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Objectives
Cytomegalovirus (CMV) infection is the most common viral agent of congenital infections and a leading nongenetic cause of sensorineural hearing loss (SNHL). The viral and immunologic factors that render developing foetus prone to SNHL are not well defined. The aim of this study was to evaluate polymorphisms in cytokine genes in relation to hearing outcome in children with congenital CMV infection (cCMV).

Methods

DNA samples from 548 children (96 with confirmed cCMV and 452 uninfected at birth) were included. Children were assessed clinically and underwent universal hearing screening by transient oto-acousting emission test performed in the neonatal period. SNHL was defined as air conduction thresholds > 25 dBHL on auditory brainstem response with normal bone conduction thresholds and normal middle ear function. A panel of 11 candidate single nucleotide polymorphisms (SNPs): TNF-alfa -1031 T/C (rs1799964), TNF-alfa -308 G/A (rs1800629), TNFRI -201 C/A (rs4149570) IL-1beta -511 C/T (rs16944), IL-1beta +3954 C/T (rs1143634), IL-10 -1082 A/G (rs1800896), IL-10RA +5964 C/T (rs4252270), IL-12B (rs3212227), MCP1 -2518 A/G (rs1024611) MCP1 +1543 C/T (rs13900), CCR5del32 (rs333) were determined in all children (by real-time PCR allelic discrimination assay, RFLP-PCR or PCR) and related to the outcome.

Results Twenty six out of 548 children failed initial hearing screening test and have confirmed SNHL in at least one subsequent hearing evaluation. Twenty four out of 26 children with SNHL at birth were congenitally infected with CMV and remaining two were CMV-uninfected at birth. When children with SNHL at birth were compared with children with normal hearing, significant association was observed for polymorphism within MCP1 gene encoding Monocyte Chemoattractant Protein 1. Increased frequencies of minor TT and heterozygous CT +1543 MCP1 genotypes were found in SNHL group compared to children with normal hearing (73.1% vs 47.6%, OR = 3.01, 95%CI: 1.24 – 7.28, $p < 0.0094$). This association remained significant after adjusting by congenital CMV, mother age at delivery, mother's CMV status and small for gestational age (OR = 3.39, 95%CI:1.32 – 8.73, $p = 0.0075$). Genotype distribution of the remaining investigated SNPs did not show any significant differences.

Conclusion

Polymorphisms in MCP1 gene may influence the risk of CMV-related SNHL, although the mechanisms underlying this effect needs to be clarified.