Etiopathogenesis of stapes fixations

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SUMMARY

Background: The etiopathogenesis of stapes fixations is different, one of them still remained unclear. Otosclerosis is a bone remodelling disorder of the human otic capsule, that leads to progressive and sensorineural heranig loss as a consequence of stapes footplate fixation and cochlear bone resorption with endosteal involvement. **Materials and methods:** This study based on three experiment: **1.** Stapes footplates were analyzed by histopatological and molecular biological methods. Nucleic acids were extracted. Measles virus was detected by nucleoprotein RNA-specific RT-PCR. Alteratively spliced RNA of CD46 isoforms was amplified by RT-PCR; cDNA amplimers were separated by poly-acrylamide gel electrophoresis and were purified from the gel. Amplimers of CD46 isoforms was restricted by endonuclease enzymes having CD46-specific recognition sites. Anti-measles IgG serum levels were measured by ELISA. **2.** Stapes footplates were analyzed by haematoxylin-eosin staining and TNFRI/II specific immunofluorescent assay was performed. **3.** Stapes footplates were analyzed by haematoxylin-eosin staining and hCIAP1/2 and Granzyme-β specific immunofluorescent assays were performed. **Results:** The presence of measles virus was associated only with the histological diagnosis of otosclerosis. All specimens were characterized by the expression of five CD46 variants (c, d, e, f and one unknown isoform). Otosclerotic specimens were featured by increased expression levels of variant ’f’ and the unknown isoform. Anti-measles IgG levels were lower in the sera of patients with otosclerosis in contrast to the nonotosclerotic stapes fixations. Active otosclerosis was featured by increased expression of TNFRII and moderate expression of TNFRI; inactive cases were characterized by permanent expression of TNFRI; however, TNFRII-specific immunoreaction was absent. Nonotosclerotic stapes specimens showed a negligible TNFR expression. Active otosclerosis was featured by robust expression of hCIAP1/2 and negligible expression of Granzyme-β. Inactive cases of otosclerosis showed inverse reaction: Granzyme-β was highly expressed; however, hCIAP1/2 specific immunoreactions were absent. Nonotosclerotic and normal stapes specimens showed no considerable Granzyme-β expression and moderate hCIAP1/2 expression. **Conclusion:** Increased expression levels of the variant ’f’ and the unknown shorter isoform as well as the special CD46 expression pattern of the human otic capsule might produce modified or pathological intracellular signalization that could create the possibility of persistent measles virus infection. Detection of elevated TNFR expression demonstrates activated osteoclast metabolism and inflammatory pathways in otosclerosis. Detection of the inversely expressed apoptosis inhibitors and inducers in active and inactive stages of otosclerosis demonstrates pathologic regulation of cell survival and apoptosis.

Keywords: Otosclerosis, CD46, TNF-α, apoptosis

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