Microglia in Meniere’s syndrome

A. Eckhard¹, F. Santos¹,², A. DiStadio¹, J. O’Malley¹, M. J. McKenna¹,²
¹ Department of Otolaryngology, Massachusetts Eye and Ear Infirmary, Boston, MA, USA
² Department of Otology and Laryngology, Harvard Medical School, Boston, MA, USA

Introduction

Microglia or resident macrophages are phagocytic sentinels in the CNS and in sensory organs, such as the retina, where they mediate neuronal homeostasis and innate immune defense. Chronic microglial activation is a common feature in a host of neuropathologic and neurodegenerative diseases, e.g. multiple sclerosis, Parkinson’s disease, and retinal dystrophies. Recently, the abundant presence of microglia/macrophages in almost all tissue compartments of the human inner ear was described, suggesting a pivotal role of ABC-diffusely distributed immune cell population for inner ear homeostasis.

Statistical significances were calculated using a one-way analysis of variance (ANOVA) and the Tukey’s honestly significant difference (HSD) post hoc test (GraphPad Prism, V6.00). GraphPad Software, La Jolla CA, USA.

Materials & Methods

Archival temporal bone sections (20 μm) from 4 individuals with a clinical diagnosis of Meniere’s syndrome and from 2 individuals without a history of otologic disease were used in this study. Cellomin was removed from mounted tissue sections with a mixture of sodium hydroxide and methanol[1], and the sections were subsequently rehydrated to water, blocked with 5% normal horse serum, and incubated with primary antibodies against IBA1 and CD163 that were raised in rabbit and in mouse, respectively. Primary antibodies were visualized either with a biotinylated secondary antibody and an ABC/DAPI detection method, or with appropriate fluorescent secondary antibodies. Images were acquired using a Olympus BX51 microscope equipped with a DP70 camera, and a Leica SP5 confocal microscope, respectively.

Results

The numbers of IBA1+ and IBA1+/CD163+ microglia/macrophages in different tissue compartments of the inner ear were significantly reduced in all four Meniere’s cases (Meniere #1 - #4) compared to the two age-matched control cases (Control #1 and #2). In particular, in the compartment of the lateral wall (stria vascularis + spiral ligament) and in the region of the organ of Corti and the basilar membrane the microglia/macrophage cell population was markedly reduced in the Meniere’s cases. Notably, these tissue compartments also exhibited a pronounced degree of tissue degeneration and an overall loss of cellularity – in particular in the apex of the cochlea. No significant differences were detected in the fraction of ‘activated’ microglia/macrophages among the investigated cases. Images show qualitative examples of the overall tissue morphology (images taken from DAB-stained sections).

Examples of IBA1+/CD163+ “activated” and IBA1+/CD163- ‘non-activated’ microglia/macrophages in different tissue compartments of the inner ear (A: Organ of Corti (+, inner and outer hair cells); B: Spiral ligament; C: Saccule; D: Stria ganglion; Scale bars: 50 μm).

Discussion

Meniere’s disease is a chronic progressive disease of the inner ear. So far, no consistent pathomorphological correlate has been identified in archival human temporal bones from Meniere’s patients, which can conclusively explain the clinical symptomatology of this disease. In particular, the sensory and neural cell populations in the inner ears from Meniere’s patients are often well preserved and do not correlate with the degree of functional impairment of the auditory and vestibular sense organs.

In the present study we therefore focused on the more diffusely distributed microglia/macrophage population that potentially has important non-immunostaining functions in the inner ear. We revealed a significant reduction of this cell population in the auditory and vestibular portions of the inner ears from Meniere’s patients; however, we did not detect any changes in the fraction of ‘activated’ (IBA1+/CD163+) microglia/macrophages.

These results suggest that Meniere’s disease is associated with a relative loss of microglia/macrophages in the inner ear. Further studies are required to clarify if the loss of microglia/macrophages is causative for the degenerative loss of other cellular elements in the inner ears – in particular in the cochlear apex – of Meniere’s patients.

Conclusions

- The microglia/macrophage populations in the inner ear is reduced in cases of Meniere’s disease. This exhibit overall degenerative changes in the auditory and vestibular sense organs.
- CD163 as a marker for microglia/macrophage ‘activation’ did not reveal any evidence for a chronic activation or over-activation of this cell population in the inner ears from Meniere’s patients.
- The relative loss of microglia/macrophages in the inner ears from Meniere’s patients requires further investigation in order to reveal its potential significance for the pathophysiology and the progressive nature of this disease.

References


Acknowledgments

Thank you to the MEED Pathology lab for their expert preparation of temporal bone specimens utilized in this study. This study was supported by NIDCD (Grant U24 DC011943).

Funding

This study was supported by NIDCD (Grant U24 DC011943).