Microglia in Meniere's syndrome

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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 microglia 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 [1], suggesting a pivotal role of this diffusely distributed immune cell population for inner ear homeostasis.
In this study we quantitatively compared the microglia/macrophage population in the inner ears from patients with Meniere's syndrome and healthy age-matched controls by immunohistochemical labeling of the microglia/macrophage marker IBA1 (ionized calcium binding adaptor molecule 1). Furthermore, we determined the fraction of "activated" microglia/macrophages by co-labeling of IBA1 and CD163 (scavenger receptor for the hemoglobin-haptoglobin complex).

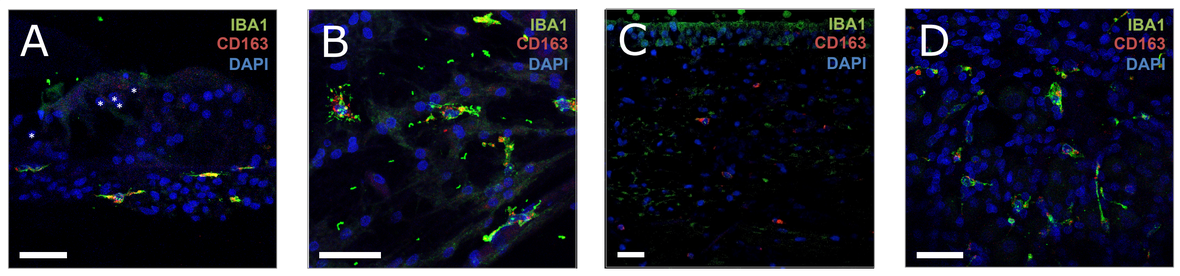
Study Goal

To identify pathologic changes in the population density and the activation state of inner ear microglia/macrophages in Meniere's syndrome by comparing the numbers of activated ($IBA1^+/CD163^+$) and non-activated ($IBA1^+/CD163^-$) microglia/ macrophages in different regions of the inner ears from patients with Meniere's syndrome and normal controls.

Materials & Methods

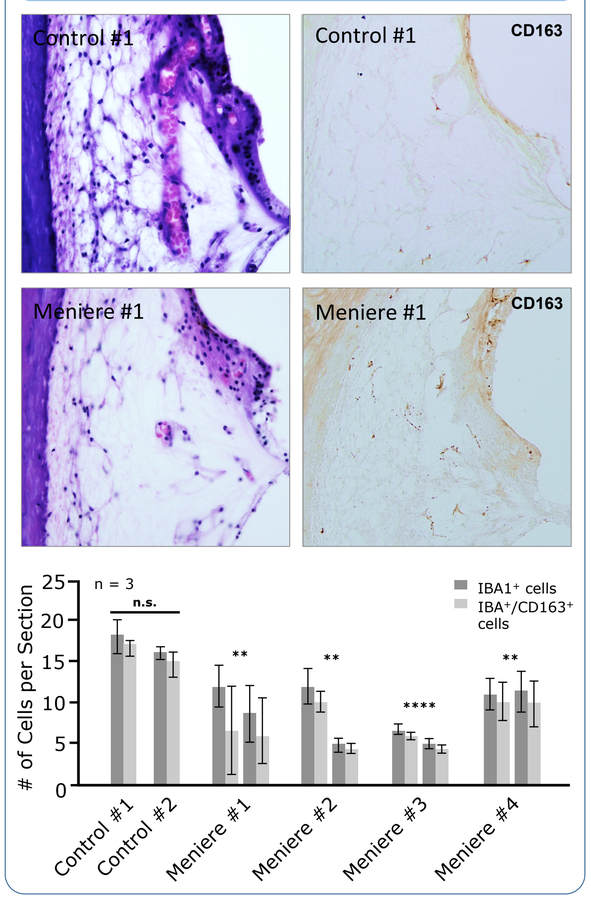
Archival temporal bone sections (20 µm) from 4 individuals with a clinical diagnosis of Meniere's syndrome and from 2 individuals without a history of otologic disease were used in this study. Celloidin was removed from mounted tissue sections with a mixture of sodium hydroxide and methanol[2], and the 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/ DAB 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.
Numbers of $IBA1^+$ and $CD163^+$ cells were counted on three non-consecutive immunolabeled sections from each case. Counting was performed by two independent investigators.
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).

Results

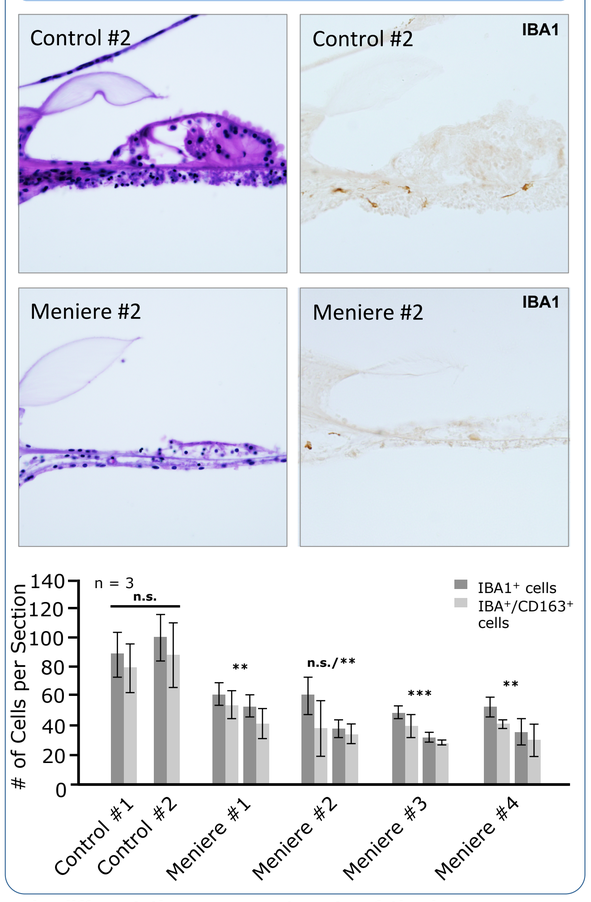


Examples of $IBA1^+/CD163^+$ "activated" and IBA1+/CD163- xxx microglia/macrophages in different tissue compartments of the inner ear (A: Organ of Corti (*, inner and outer hair cells); B: Spiral ligament; C: Saccule; D: Spiral ganglion; Scale bars: 50 µm).

Stria vascularis + Spiral ligament

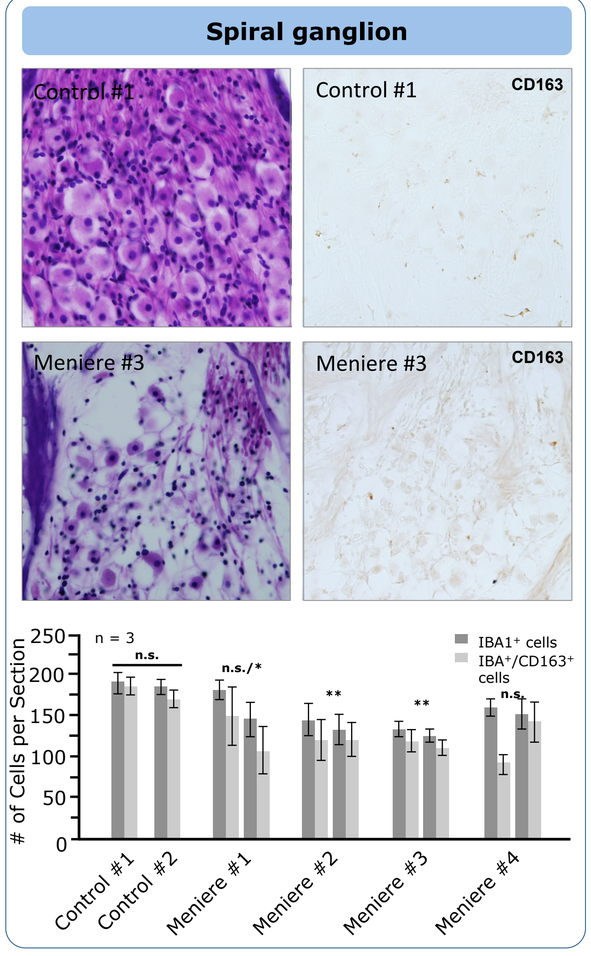


Organ of Corti

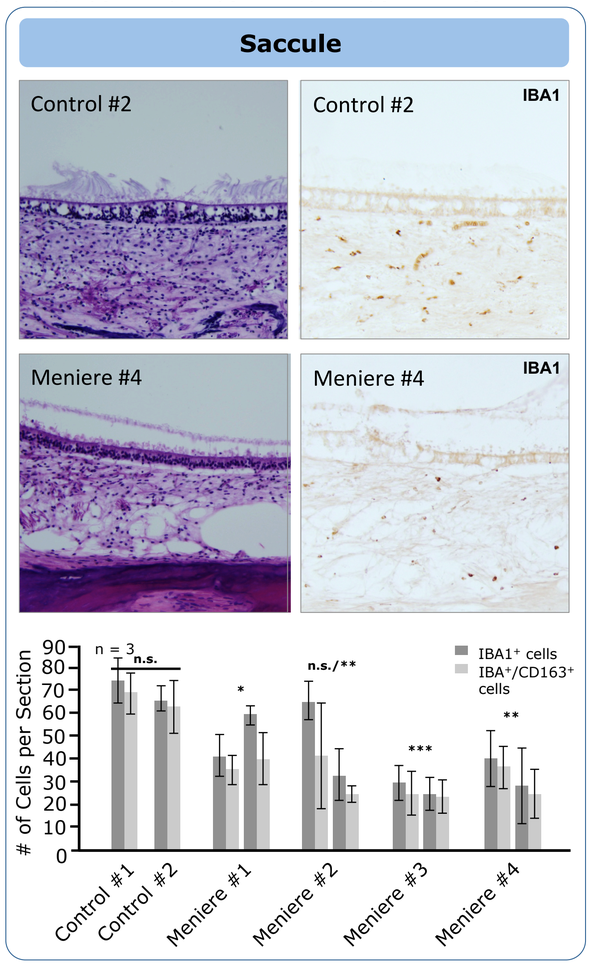


The numbers of $IBA1^+$ and $IBA^+/CD163^+$ microglia/macrophages in different tissue compartments of the inner ear were significantly reduced in all four Meniere's cases ('Meniere #1 – #4') compared to the two age-matched control cases ("Control #1 and #2'). In particular, in the compartment of the 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 $IBA^+/CD163^+$ cells among the investigated cases. Images show qualitative examples of the overall tissue morphology (images taken from hematoxylin-eosin (HE) stained sections) and the immunolabelings for IBA1 and CD163 (images taken from DAB-stained sections). (n.s., no significant difference; *, p<0.05; **, p<0.01; ***, p<0.001; ****, p<0.0001).

Spiral ganglion



Saccule



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 sympto-matology 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 homeostatic 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 that 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

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