

Letters

Inner ear involvement in multiple sclerosis: An underestimated condition?

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The interest of the scientific community for associated symptoms in multiple sclerosis (MS) has grown in the last years. Audio-vestibular manifestations such as sudden sensorineural hearing loss (SSNHL) and acute vertigo are often reported in patients with MS; such conditions are mainly attributed to demyelination of the vestibulocochlear nuclei and temporal lobe, while the involvement of the vestibulocochlear nerve and inner ear is still debated and underestimated.¹

Hearing impairment that mainly present as SSNHL, affects between 1% and 17% of MS patients¹ and is commonly attributed to central nervous system demyelination. Vertigo affects from 7% to 30% of patients² and is mostly attributed to demyelination of the vestibular nuclei, musculoskeletal weakness, and ocular diseases rather than to the labyrinth or vestibular nerve. However, there is growing pathophysiological evidence of the involvement of the inner ear and vestibulocochlear nerve in hearing loss and vertigo in MS patients.

The evidence of a unequivocal presence of macrophages in human temporal bones of patients with autoimmune disease, even at early stages of the disease,³ supports the hypothesis that autoimmunity mechanisms in MS may also affect the inner ear; hair cells and auditory and vestibular spiral ganglion neurons may be subject to the attack of lymphocytes, and the resulting damage may manifest with SSNHL and acute vertigo.

Microglia, in its M1 phenotype, has been considered playing an important role in the processes of demyelination in MS. Temporal bone studies have identified microglia in the cochlea, showing its migration into the Internal Auditory Canal (IAC) until the inner ear.⁴ M1 phenotype microglia could demyelinate cochlear and vestibular structures causing SSNHL or acute vertigo; such episodes may be temporary due to the relapsing–remitting phases of MS that alternatively activate the two different microglia phenotype (M1↔M2).

The microglia demyelinating action on brain and medulla has been shown as White Matter Hyperintensities (WMH) in Magnetic Resonance Imaging (MRI) of patients with MS. The presence of WMHs in the IAC and in the cochlea has been previously demonstrated;⁵ this supports the hypothesis that audiovestibular symptoms may be related to the effects of microglia on peripheral audiovestibular structures. Unfortunately, MRI does not have enough sensitivity to identify demyelization processes in the inner ear; such involvement could be instead explored with specific electrophysiological tests that are routinely used in audiological examination such as Auditory Brainstem Responses (ABR) and Vestibular Evoked Myogenic Potentials (VEMPs).

The role of the inner ear and vestibular cochlear nerve thereby determining hearing loss and vertigo in patients with MS is supported by current evidence. Audiovestibular symptoms in young subjects, especially when spontaneous recovery occurs, could represent an early sign of MS even when no demyelinated plaques are visible in the central nervous system; these subjects should always be evaluated with clinical, radiological, and electrophysiological tests to exclude peripheral incipient MS.


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Acute exacerbations after decades of non-active chronic multiple sclerosis

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Dear Editors,

Despite a growing number of medications effective against relapses and magnetic resonance imaging (MRI) activity in remitting–relapsing multiple sclerosis (RRMS), still probably half of the persons with multiple sclerosis (MS) worldwide have reached progressive phases of multiple sclerosis (PMS), a majority of them with non-active appearance.¹ As disease modifying drugs (DMD) mostly have not proven beneficial in this stage, they are not recommended after onset of progressive non-active stages. Natural history studies report cessation of relapses as patients go through the secondary progressive stage. At present, discontinuation of previously prescribed DMDs in later stages of MS is under discussion.² We report on two female MS patients, aged 61 and 67 years, who experienced unexpected acute clinical MS exacerbations after decades of chronic non-active disease which were confirmed on MRI.

Case 1 had been diagnosed with RRMS 41 years ago. She had not been on DMD therapy before admission. After three decades of a “chronic progressive, non-active” course, she presented with an increase in her paraparesis, marked fatigue and abrupt cognitive deterioration. Her Expanded Disability Status Scale (EDSS) was 7.5. Cranial MRI showed four active gadolinium-enhancing lesions in the parietal deep white matter bilaterally. She was treated with high-dose intravenous corticosteroid therapy and improved.

Case 2 had been diagnosed with MS 42 years before. She had been on interferon beta 1 a (IFN beta-1a)

22 mcg sc tiw during the last 13 years. IFN had been stopped 3 months before admission as neutralizing antibodies (NAb) against IFN were demonstrated and confirmed. She presented an acute exacerbation with a pronounced left-sided spastic tetraparesis and severe fatigue. Spinal MRI showed gadolinium-enhancing T1 lesions in her cervical cord. EDSS was 6.5. She received an intravenous corticosteroid pulse and experienced walking improvement.

In both cases, no additional trigger factors (viral infections, comorbidities, etc.) except withdrawal of DMD treatment in the presence of neutralizing anti-drug antibodies in the second case were found. Both cases depict the problem of longstanding clinical appearance as “non-active” chronic progressive MS. Fatigue may be an additional indicator of immunological activity besides new motor and sensory symptoms which are probably often masked in longstanding paraparesis or tetraparesis. Occurrence of acute exacerbations after decades of an apparently progressive course is unusual and adds questions to the rationale of DMD withdrawal in PMS. A new spectrum of MS reactivations may arise after cessation of DMDs.³

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