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Correlation Between Laterality of Hearing Loss and Migraine Features in Meniere's Disease

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Abstract

Objectives: To understand whether the hearing loss laterality in Meniere's disease (MD) correlates with migraine symptoms laterality such as headache, neck stiffness, and otalgia.

Methods: We performed a retrospective review of prospectively obtained data on patients presenting between September 2015 and October 2021 with definite or probable MD. A custom-designed, comprehensive questionnaire was used to identify patients' migraine-related symptoms. The clinical and audiometric data were used to diagnose patients with definite or probable MD using criteria set by the American Academy of Otolaryngology-Head and Neck Surgery.

Results: In total, 113 patients with definite or probable MD were included in the study. The mean age of the patients was 60 ± 15 years with no gender predominance (49.6% male and 50.4% female). A total of 57 (50%) patients were presented with headaches. Among the migraine-headache cohort, headache and otalgia were on the same side as the MD ear affected by hearing loss. In addition, in patients who present with otalgia as the primary feature of headache, otalgia was more likely to be on the same side as the ear affected by the hearing loss.

Conclusion: The high prevalence of migraine symptoms on the same side of the ear affected by MD among this cohort could suggest a shared pathophysiology in both MD and migraine, possibly involving migraine-related changes in both the cochlea and vestibule.

Keywords

Migraine; Meniere's Disease; Headache; Otalgia; Hearing Loss; Otologic Migraine

Introduction

Meniere's disease (MD) is a clinical syndrome that Prosper Meniere first described in 1861.[1] It is characterized by a symptomatic triad of episodic vertigo, tinnitus/aural fullness, and fluctuating sensorineural hearing loss.[2] MD is estimated to affect 190 cases per 100,000

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in the United States alone.[3] The Classification Committee of the Bárány Society, along with several international organizations, have officially defined diagnostic criteria for MD.[4] However, these criteria do not include migraine headaches, the fourth symptom described in the original work of Meniere.[5] Although the pathophysiology of MD is not well understood, various theories have been proposed. The latest understanding of the disease suggests that central action and resultant neurovascular changes in the inner ear might be the etiology behind MD.[6]

Migraine headaches are found to be associated with a variety of otologic symptoms such as recurrent benign paroxysmal positional vertigo,[7] mal de debarquement,[8] vestibular migraine,[9] tinnitus, aural fullness,[10] otalgia,[11] and recently sudden sensorineural hearing loss.[12] In addition, migraine headaches or atypical migraine symptoms are frequently found in association with MD (Figure 1).[13] Recent studies have started to investigate the epidemiological and mechanistic association between MD and migraine, as a study had shown that 56% and 85% of patients with unilateral and bilateral MD, respectively, had migraine.[14] Ghavami *et al.* found a migraine prevalence of 51% in patients with definite MD and the rest of the 49% had either a family history of migraine in a first degree relative or multiple migraine-related symptoms.[13] Radtke *et al.* also recognized an increased prevalence of migraine in the MD group (56%) when compared to a matched control group (25%). Furthermore, 28% of these patients experienced migrainous headaches during their Meniere attacks.[15] Neurovascular crosstalk between the vestibular system and the trigeminal nerve and dysregulation in ion channels in the inner ear might be the underlying causes of migraine and MD; thus, predisposing the favorable effects of migraine medications in MD patients.[6,16,17,18]

In this study, we aim to assess whether patients with MD, who suffered or did not suffer from migraine headache, manifested migraine symptoms (headache, neck stiffness, and otalgia) on the same side of the ear affected by hearing loss. These findings will further highlight the association between MD and migraine.

Materials and Methods

Following Institutional Review Board approval, we performed a retrospective chart review of patients who presented to a tertiary-care neurotology clinic, between September 2015 and October 2021 and were diagnosed with MD. During their first visit, these patients were provided with a comprehensive questionnaire as part of our routine clinical assessment process, and their responses were recorded in a secure clinical database (Redcap, Vanderbilt University, Nashville, TN, USA). The questionnaire was used to identify the occurrence, frequency, and laterality of migraine-related symptoms, including headache (which could have occurred before, during, or after MD episodes), neck pain or stiffness, and otalgia. In the questionnaire, we specifically differentiated between otalgia, which was defined as a sharp or dull pain in the ear, and aural pressure, which referred to a sensation of fullness or ears feeling clogged that did not resolve with ear popping. Furthermore, to minimize confounding factors, we excluded headache, neck pain or stiffness, and otalgia that were attributed to other known causes such as cervical spine arthritis, ear infection, temporomandibular joint disorders, etc. The clinical and audiometric data were used to

diagnose patients with definite or probable MD using criteria set by the American Academy of Otolaryngology-Head and Neck Surgery. Migraine headaches were diagnosed using the criteria set by the International Classification of Headache Disorders (ICHD-3).[19] To investigate whether the laterality of hearing loss was related to the laterality of an otologic symptom, a Chi-squared analysis was used. This analysis was applied to all patients, as well as the subsets of those who suffered or did not suffer from headaches. Statistical analysis was performed using R version 4.2.0 software with a p-value less than 0.05 considered statistically significant. Bonferroni correction was applied to reduce the occurrence of type I errors.

Results

In total, 113 patients with MD were included in this study, with a mean age of 60 ± 15 years. The population was evenly split in gender, with 56 (49.6%) males and 57 (50.4%) females. We categorized our patients into three subgroups: patients without headaches, patients with headaches who fulfilled the ICHD-3 migraine criteria, and patients with headaches who did not fulfill these criteria. Among all patients, 57 (50%) had headaches, 18 (16%) had neck pain or stiffness, and 27 (24%) had otalgia. Patients who suffered from headaches were evaluated for ICHD-3 criteria. Among all 57 patients who reported headaches, 33 (58%) patients fulfilled the ICHD-3 criteria. The remaining 24 (42%) patients did not fulfill the ICHD-3 criteria.

Among all patients, headache and otalgia were on the same side as the ear affected by the hearing loss (p<0.001). However, neck pain or stiffness did not demonstrate any correlations (p=0.44) (Table 1). Among the non-headache cohort, the laterality of hearing loss coincided with the side of otalgia (p=0.03). Neck pain and stiffness showed no trends (Table 2). Within the patients who suffered from migraine headaches, the laterality of hearing loss with headache (p<0.001) and otalgia (p=0.04) were correlated. Conversely, neck pain and stiffness (p=0.12) showed no relation (Table 3).

Discussion

Our retrospective study of 113 patients with MD, demonstrated a high incidence of migraine headaches (29%) in patients with definite or probable MD compared to the prevalence of migraine headaches in the general population (15%).[20] This finding provide evidence of an epidemiological association between MD and migraine – that was also described in other studies.[14,13,15] In a large case-control analysis of 514,866 patients, Kim *et al.* demonstrated a bidirectional association between migraine and MD. Within this cohort, 24.7% of MD patients had a history of migraine and 5% of migraine patients had a history of MD.[17]

Among the non-headache cohort, patients frequently experienced otalgia on the same side that was affected by hearing loss (p=0.03). This finding suggests that migraine can present with many different symptoms other than a typical headache, such as in this case where patients presented with otalgia as a primary feature of headaches.[21,22] In fact, studies have shown a bidirectional epidemiological association between migraine headache and otalgia.[11] Teixido *et al.* found that 77% of patients who presented with otalgia as a primary complaint

had a history of headache, with 65% of them meeting the migraine headache criteria set by the International Headache Society. Moreover, in 65% of patients, otalgia was triggered by typical migraine triggers such as certain food, pressure changes, and noise. Additionally, when these patients were treated with migraine treatment, 92% of them showed at least a 50% reduction in the frequency, severity, or duration of their otalgia.[22] On the other hand, among patients suffering from migraine, the high prevalence of migraine symptoms – headache ($p<0.001$) and otalgia ($p=0.04$) – on the same side of the MD ear affected by the hearing loss suggests a pathophysiological association between MD and migraine.

The pathophysiology of MD has not been clarified yet. Since Yamakawa[23] and Paparella and Djalilian,[24] endolymphatic hydrops (EH) have been regarded as the histopathologic feature causative of MD. Multiple factors, such as excessive production or decreased absorption of endolymph in the cochlea and vestibular system, vascular changes,[25,26] membrane rupture theory,[27,28] electrolytes imbalance,[29] and aldosterone-induced EH[30] have been proposed to cause EH. Furthermore, the American Academy of Ophthalmology and Otolaryngology incorporated this central hypothesis in its definition of MD.[31] However, in 1989, Rauch *et al.* published a noteworthy article that questioned the validity of EH being the underlying cause behind MD. In their postmortem temporal bone study, they demonstrated that all temporal bones of patients with clinical MD had EH in at least one ear. However, the reverse was not true, as six temporal bone specimens that had idiopathic EH didn't manifest MD.[32] These results were similar to those found in later studies conducted by Merchant *et al.*[33] and Foster and Breeze.[34] These findings are consistent with EH being an epiphenomenon rather than the cause of symptoms in MD; thus redirecting the research towards other potential factors.

Migraine is considered one of the most essential factors of MD based on the aforementioned epidemiological connection and common pathophysiology (described below) with MD. Migraine is caused by cortical spreading depolarization that activates the trigeminocervical complex. The sensitization of the trigeminovascular pathways leads to the release of vasoactive neuropeptides and cytokines such as calcitonin gene-related peptide, neurokinin A, and substance P causing vasodilatation.[6,35,36] This abnormal activation of the trigeminal meningeal nociceptors and secretion of the trigeminal nerve results in a chronic neuroinflammatory state in the intracranial meninges that leads to pain in migraine patients. Moreover, the vestibule and cochlea are connected to the trigeminal nervous system via neurovascular branches that mediate the vascular effects of migraine on the inner ear.[17] Subsequently, cortical spreading depolarization, altered central processing in the vestibular and auditory cortices, inflammation of the trigeminal nerve, and vasospasm of the posterior cerebral arterial circulation underlie the mechanism of migraine-related vestibular (vertigo, dizziness, imbalance, mal de debarquement) and cochlear symptoms (tinnitus, otalgia, aural fullness, and sudden hearing loss).[37] Despite being underdiagnosed, vestibular migraine has been recognized and its criteria were formalized by the Bárány Society and the International Classification of Headache Disorders.[38] On the other hand, cochlear migraine is still a new concept that was first described by Lai and Liu[39] and further supported by Hwang *et al.*[40]

MD patients display features that encompass vestibular migraine and cochlear migraine symptoms. In ears with EH, the autoregulation of the blood flow is impaired making them vulnerable to stress factors – such as those present in migraine – and more likely

to develop MD.[6] In fact, in several studies of animals, authors have demonstrated that a dysfunctional cochlear blood flow (decreased blood flow or increased blood viscosity) results in inner ear dysfunction symptoms.[41,42,43,44] Treatment of MD is complex due to the lack of understanding of the pathophysiology of MD and the challenges in designing a clinical trial for MD patients. Therefore, there are no FDA-approved medications for MD and there is no cure to stop the progression of the damage to the inner ear. However, several studies demonstrated that patients with MD have responded to migraine diet and lifestyle modifications, as well as a combination of migraine medications. These patients reported control of their vertigo, stabilization of their hearing loss, and improvement in their quality of life.[6,13,16,18] These outcomes further suggest a correlation between MD and migraine.

This study is limited by its sample size as it was performed at a single tertiary neurotologic clinic. In addition, some patients have experienced their symptoms months prior to their appointment which could introduce recall bias, while other patients had more recent attacks close to their appointment and therefore better recall. However, we tried to limit this bias by referring to patients' medical records. Finally, a larger prospective study would help further explain the association between migraine and MD, but for now by recognizing this link physicians will help treat patients with MD.

Conclusion

A high prevalence of patients with MD had migraine headaches as defined by ICHD-3 migraine criteria. MD patients who did not have headaches had atypical ear pain associated with migraine. Therefore, our findings support an epidemiological and etiological association between MD and migraine. MD may be part of the spectrum of otologic migraine, where migraine manifests primarily as otologic symptoms. We recommend that patients with MD and migraine receive migraine treatment prior to destructive therapy.

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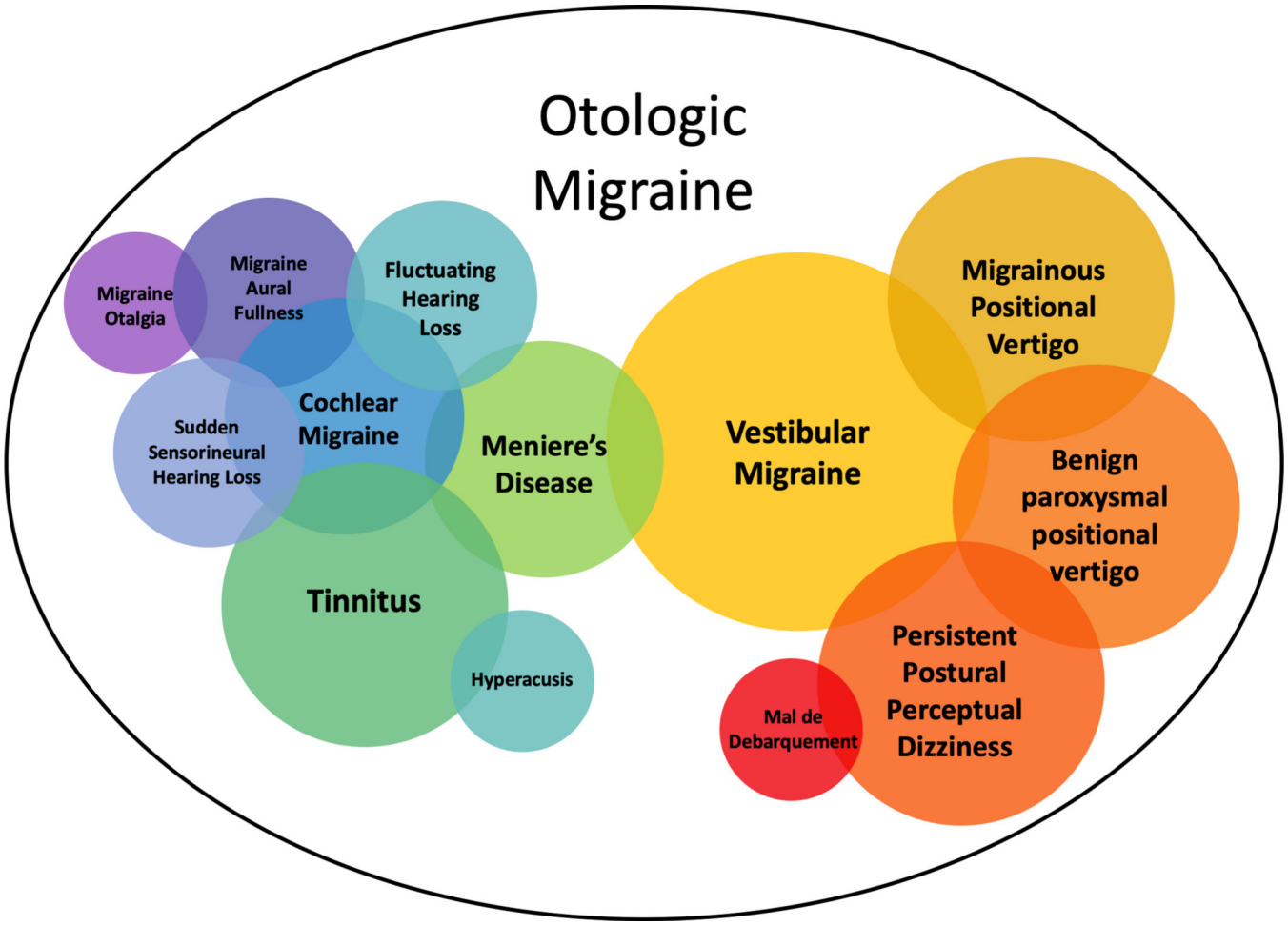

Figure 1.
Venn Diagram Showing the Interconnection Among Migraine-Related Cochlear and Vestibular Symptoms and Disorders.

Table 1.

The Correlation of Migraine Features Laterality to Hearing Loss Among the Entire Cohort with Meniere's Disease

Feature	Right-sided MD (N=30)	Left-sided MD (N=33)	Bilateral MD (N=50)	*p* Value	p_c Value
Headache on Same Side or Bilateral	7 (23%)	6 (18%)	23 (46%)	<0.001 *	<0.001 *
Neck Pain or Stiffness on Same Side or Bilateral	0 (0%)	2 (6%)	5 (10%)	0.44	-
Otalgia on Same Side or Both Ears	4 (13%)	9 (27%)	11 (22%)	<0.001 *	<0.001 *

* Denotes a significant p and p_C value

p_C value indicates Bonferroni's correction

Table 2.

The Correlation of Migraine Features Laterality to Hearing Loss Among the Non-Headache Cohort with Meniere's Disease

Feature	Right-sided MD (N=13)	Left-sided MD (N=16)	Bilateral MD (N=27)	*p* Value	p_c Value
Neck Pain or Stiffness on Same Side or Bilateral	0 (0%)	0 (0%)	0 (0%)	0.56	-
Otalgia on Same Side or Both Ears	4 (31%)	5 (31%)	0 (0%)	0.01*	0.03*

*Denotes a significant *p* and p_C value

p_C value indicates Bonferroni's correction

Table 3.

The Correlation of Migraine Features Laterality to Hearing Loss Among the Migraine Headache Cohort with Meniere's Disease

Feature	Right-sided MD (N=10)	Left-sided MD (N=8)	Bilateral MD (N=15)	*p* Value	p_c Value
Headache on Same Side or Bilateral	4 (40%)	4 (50%)	15 (100%)	<0.001 *	<0.001 *
Neck Pain or Stiffness on Same Side or Bilateral	0 (0%)	2 (25%)	5 (33%)	0.12	-
Otalgia on Same Side or Both Ears	3 (30%)	1 (13%)	5 (33%)	0.01 *	0.04 *

* Denotes a significant p and p_C value

p_C value indicates Bonferroni's correction