THE CHALLENGE OF VESTIBULAR MIGRAINE

Author: Eric W. Sargent, MD, FACS

Affiliation: Michigan Ear Institute, Farmington Hills, MI

Address: 30055 Northwestern Highway, #101, Farmington Hills, MI 48334

Abstract

Purpose of review: Migraine is a common illness and migraine-related dizziness occurs in up to 3% of the population. Because the diagnosis is controversial and may be difficult, many patients go undiagnosed and untreated. This review summarizes current understanding of the taxonomy and diagnosis of vestibular migraine (VM), the relation of VM to labyrinthine disease, and the treatment of the condition in adults and children.

Recent findings: The categories of migraine accepted by the International Headache Society (IHS) do not reflect the complex presentations of patients suspected of having VM. In clinical practice and research, criteria are increasingly accepted that divide patients suspected of VM into 'definite VM' and 'probable VM.' Because vertigo itself may trigger migraine, patients with VM should be suspected of having vestibular end-organ disease until proven otherwise. Treatment remains controversial because of a notable lack of randomized controlled studies of VM treatment.

Summary: For now, the best strategy for the treatment of suspected VM patients is dietary/lifestyle modification, anti-nausea/anti-emetics for acute vertigo, and preventive medication for patients who have continued disruptive symptoms. Patients with VM should be monitored regularly for the development of latent audio-vestibular end-organ disease.

Introduction

Affecting 15 - 17% of women and 6% of men and 9.7% girls and 6.0% boys under 20, migraine is a common condition that affects people of all ages and races. Dizziness is a common association of migraine in many patients and 'migraine-associated dizziness' or 'migraine-associated vertigo' occurs in 1 - 3% of the population. [1] However, because of its protean manifestations, the diagnosis of migraine-associated dizziness may be difficult to make and outcomes of treatment difficult to assess. Names used to describe the condition reflects the complexity, with three terms commonly used: migraine-associated dizziness, vestibular migraine (VM), and migrainous vertigo.[2] The situation is aptly represented in the story of the blind men and the elephant: each had his own perception of the animal depending on which part was touched. In the same way, separate disciplines that deal with dizziness - chiefly neurology and neurotology - have come up with sometimes conflicting views of this condition. As a result of these factors, the condition is under-diagnosed and under-treated.

Definition and Classification

Vertigo is "the sense of self-motion when no motion is occurring or the sensation of distorted self-motion during an otherwise normal head movement."[3] The breadth of this definition is important in VM because the condition may not manifest classic horizontal- or torsional rotatory vertigo of peripheral vestibular disease. While

3

sometimes a horizontal-rotatory sensation, the vertigo of migraine is often a 'to-and-fro'-type sensation.

Some suggest that "migrainous vertigo" be used to describe episodes of vertigo that accompany other migraine features and "migraine-associated vertigo" be used to refer to vertigo spells in patients with a history of migraine, but who don't necessarily have migraine features at the time of the spells.[2]

Migraine is classified by the International Headache Society (IHS) in the International Classification of Headache Disorders, 2nd edition (ICHD-II).[4] Types of migraine include 'migraine with or without aura', 'migraine with prolonged aura', 'basilar migraine', 'migraine aura without headache', 'childhood periodic syndromes', 'Benign Paroxysmal Vertigo (BPV) of childhood', and 'migrainous infarction.' Under this system, vestibular symptoms are only recognized in basilar-type migraine and BPV of childhood. While looser references to dizziness are included with other headache criteria, most clinicians who treat patients with VM find the ICHD-II criteria insufficiently descriptive.

The most widely-accepted classification of dizziness related to migraine are the "Neuheuser criteria." Shown in Table 1, these criteria divide VM into categories of 'definite' and 'probable' for research and clinical purposes. Earlier versions of this classification included response to anti-migraine medication or migraine precipitants of vertigo in the definition of probable VM. The most recent review of the clinical utility of the criteria has dropped these as too non-specific.[5] The classification scheme remains debated and the coherence of 'probable vestibular migraine' as a diagnostic entity has been questioned.[6]

4

A related entity, 'Chronic subjective dizziness' (CSD), is chronic unsteadiness or non-vertiginous dizziness accompanied by hypersensitivity to motion stimuli and poor tolerance for complex visual stimuli or precision visual tasks lasting for 3 months or more.[7] CSD often co-exists with recurrent vertigo syndromes, such as Ménière's Syndrome and VM, although the direct relationship is not known.[8] CSD may be the spatial sensory analogue of allodynia experienced by some chronic migraine headache sufferers.

Symptoms

In adults, 30% of patients eventually diagnosed with VM may present without headaches.[9] VM is most commonly an affliction of mid-life that preferentially affects females. While the mean age of headache onset in patients with VM is typically 28 years, the mean age of dizziness onset among patients with VM is 49 years 19-79 years) with 3:1 female preponderance.[6]

Patients with VM commonly report acute episodes of vertigo lasting seconds to days. Transient fluctuating hearing loss, aural fullness and tinnitus, and audiometrically documented mild SNHL has also been described.[10,11] Episodes lasting hours may mimic Ménière's syndrome while shorter episodes may mimic BPPV.[8]

The association of the vertigo of VM with headache in patients who suffer both is often asynchronous: only a small number of patients with VM have vertigo that presents as aura (5 - 60 minutes of sensory disturbance followed by a migraine headache). There is no consistent pattern of vestibular symptoms during active headache.[6]

Over time, VM tends to persist. Almost 90 percent of patients with definite VM still report vertigo attacks during the prior 12 months after an average observation period of 9 years. While more than half experience less frequent attacks after the observation period, about 30 percent experience more frequent attacks and almost all still have migraine headaches.[12] About 50% of patients initially diagnosed with 'probable VM' progress to 'definite VM.'[5]

Cochlear symptoms such as tinnitus, aural fullness, or hearing loss (including sudden hearing loss) during spells of vertigo are common in adults with migrainous vertigo and, as time passes, become more common. Followed for an average of 9 years, the number of patients with cochlear symptoms more than doubles.[12]

Up to 50% of childhood vertigo cases are probably related to migraine, including VM and benign paroxysmal vertigo (BPV) of childhood. BPV of childhood is the most commoncause of vertigo between 2 - 6 years of age with an estimated prevalence of 2.6% for children between 5 - 15 years of age.[13]

The typical attacks of childhood BPV include seconds to minutes of vertigo or dizziness, often associated with nystagmus, postural imbalance, nausea and vomiting. Children are usually 'normal' between attacks. Attacks vary widely in frequency and may present before age 2. In many sufferers, the condition disappears after the 6th birthday. BPV of childhood has a strong association with family history of migraine and can predict later development of typical migraine. As in adults, there is a high incidence in children of VM without headache, although the incidence is not known. In children less that 10, the presentation may be more variable than in adults.[13]

Differential Diagnosis

Some suggest that VM is the most common cause of spontaneous, recurrent vertigo in adults. It shares features with Ménière's syndrome and episodic ataxia type 2. Transient ischemic attacks, masquerading as aura without headache, must be excluded.[9] In long-term follow-up, diagnoses that may replace VM as the presumed cause of vertigo included BPPV, 'psychogenic dizziness', and spinocerebellar ataxia.[5] In the author's neurotologic practice, the most common diagnoses replacing VM are BPPV and Ménière's syndrome.

Pathophysiology

The pathophysiology of migraine in general is poorly understood and there is even less consensus on the pathophysiology of migraine-associated dizziness.[2] A detailed description of a pathophysiologic model based on currently available knowledge can be found in a recent article by Furman and Marcus.[14]

It is debated whether vestibular symptoms in migraine might be an aura (similar to the visual aura that signals spreading depression), part of the headache event, (like photophobia), caused by transient peripheral vestibulopathy, or due to another process. Based on their review of the temporal profile of vestibular symptoms, Eggers' *et al.*, suggest that vertigo in VM occurs as an ictal phenomenon (like headache or photophobia) rather than as a manifestation of spreading depression like a sensory or motor aura.[6]

'Kindling' similar to the sensitization seen in epilepsy wherein seizures lower the threshold for further seizures has been suggested as a reason for the permanent

sensitization that occurs in the trigemino-vascular pathways of chronic migraineurs.[2] A similar kindling effect may be the reason patients with VM become sensitized to certain stimuli, such as motion in their visual surround, and suffer cycles of of VM.

There are suggestions of the role of genetics in development of migrainous vertigo: in 2009 the first locus for autosomal dominant familial migrainous vertigo mapped to 5q35 was reported in a 4-generation family. In this family, the majority of vertigo sufferers had migraine headaches that preceded the vertigo by 15 - 20 years.[15]

Vertigo induced by caloric testing (and presumably also by endogenous causes) can trigger migraine. In a provocative study of 39 subjects with a history of migraine who underwent caloric testing, 19 experienced their usual migraine within 24 hours. Of these, 47% had onset of migraine during the test. Only 1 of 21 from the matched control group had a migraine during a 24-hour observational period.[16] The notion that vertigo *itself* is a trigger of migraine stands the relationship of vestibular end-organ causes of vertigo (e.g., Ménière's Syndrome, BPPV, or a static vestibular deficit that induces visual distortion during head movement) to migraine on its head. Since vertigo from a peripheral cause can be the trigger of the migraine or migraine-related symptoms the relationship in many cases may be 'vertigo-associated migraine' rather than the converse.

Associations with Peripheral Vestibular Disorders

VM is often observed in association with well-defined peripheral disorders, chiefly Ménière's syndrome and Benign Paroxysmal Positional Vertigo (BPPV).

Ménière's Syndrome

The relationship between Ménière's syndrome and VM, both chronic illnesses with episodic features, is particularly complicated. Patients frequently suffer symptoms of both conditions at different times or, in some cases, simultaneously.

In tertiary vertigo/dizziness practices (which have inherent selection bias), almost 30% of patients with Ménière's syndrome may also have VM. An additional 30% of Ménière's syndrome patients may have migrainous features, but not meet VM criteria. A combination of Ménière's syndrome and VM is not rare and must be accounted for in treatment planning.[8]

With time, more patients initially diagnosed with VM tend to develop auditory symptoms and the objective auditory signs of Ménière's syndrome. 13 - 18% of patients with initial 'definite' or 'probable' VM may develop bilateral low-frequency SNHL over a 9 year period. 7 - 11% develop hearing loss and cochlear symptoms that meet AAO-HNS criteria for bilateral Ménière's syndrome.[5, 12]

Based on these observations, the question remains: How many patients initially diagnosed with VM who later develop hearing loss typical of Ménière's syndrome actually have migraine features triggered by vertigo attacks caused by latent Ménière's syndrome - i.e., 'vertigo-associated migraine'?

The outcome of vestibular surgery for patients with a history of simultaneous migraine and intractable symptoms of Ménière's syndrome has not be well-studied. The author's review of endolymphatic sac decompression in patients with Ménière's syndrome alone and those who suffer Ménière's syndrome and migraine headaches suggests that patients with migraine and Ménière's syndrome fare far worse than

patients with Ménière's syndrome alone on quality of life measures.[17] This may be predicted by the observation that, in general, subjects with VM and co-morbid neurotologic conditions have higher levels of subjective dizziness handicap, anxiety, depression and psychological distress than subjects with VM alone.[6]

BPPV

As in Ménière's syndrome, the relationship between BPPV and VM is complicated. Patients successfully treated with the Epley maneuver for BPPV are more likely than the general population to have a history of motion sickness or migraine. Patients with subjective symptoms of BPPV who lack signs of the condition frequently have concomitant migraine.[18] It may be that the motion sensitivity commonly seen in migraineurs causes these patients to seek attention more quickly than patients without migraine or motion sensitivity when they develop BPPV.

Low-velocity, sustained nystagmus on positional testing that dissipates during symptom-free periods in patients presenting with vertigo, nausea and headache has been said to suggest VM.[19] Other studies include patients diagnosed with 'definite' or 'probable' VM who also had atypical positional nystagmus and/or vertigo in their study populations with the assumption that these symptoms and signs were probably related to migraine.[5] However, caution in these situations is warranted since this type of positional nystamus could be caused by cupulolithiasis, anterior or horizontal (or multiple) canal BPPV variants that, in turn, triggers the 'vertigo-associated migraine' alluded to earlier.

Testing

There are no findings on imaging or vestibular testing pathognomonic of VM; however, non-specific abnormalities on these tests are often observed.

Imaging

While there are no known findings on routine MRI pathognomonic of VM, there is a MRI correlate to migraine generally. Migraine sufferers are roughly 4 times more likely to have white-matter hyperintensities (WMHs) on MRI than healthy age- and sex-matched controls. The highest prevalence of WMHs occur in patients with migrainous aura.[20]

Although *in vivo* study of brain activity through functional neuroimaging has yielded insights into the pathophysiology of migraine in general, to date there are few reports of functional imaging in VM. This remains a promising area of study.

Vestibular Testing

Studies of oculomotor and caloric testing in patients with VM are inconsistent. Large studies of patients with definite or probable VM find only non-diagnostic abnormalities on neurotologic exam and vestibular laboratory testing in patients with VM as their sole diagnosis. Not surprisingly, subjects with VM and co-morbid peripheral vestibular disease (BPPV, Ménière's syndrome) are more likely to have abnormalities on testing.[6] The incidence of unilateral canal paresis on caloric testing increases with time in patients with VM and small and equal numbers of subjects demonstrate vestibular hypo-responsiveness and hyper-responsiveness.[12]

Vestibular Evoked Myogenic Potential testing in one study suggested abnormalities in the sacculocollic pathway of patients with presumed migrainous vertigo compared to healthy volunteers.[21] However, these findings have not been duplicated and the connection remains unconfirmed.

Treatment

Most VM patients probably do not receive treatment despite substantial disability. This apparent neglect is at least partially understandable because there is currently no specific treatment for VM outside of conventional migraine management.[2, 12] The first obstacle to treatment is usually patient acceptance of the diagnosis. Because vertigo or dizzy episodes in VM are often temporally independent of headache, patients may not see the logic of linkage with migraine.[22]

Acute Treatment

While occasional small studies suggest triptans may have modest benefit in some patients during acute vertigo attacks, reports on the use of triptans for vertigo in VM is inconclusive.[23] In the experience of the author, triptans in acute migrainous vertigo are rarely of benefit. Patients seldom report using the medication after an initial trial. The utility of triptans in aborting a vertigo attack is also suspect given their ineffectiveness in treating visual auras.[22] Acute migrainous vertigo in children, as in adults, does not respond well to triptans or NSAIDs.[13]

Short-term use of calcium channel blocking medications nimodipine and nifedipine is ineffective in shortening aura or preventing headache and these medications have not been used in migrainous vertigo attacks.[22]

The only treatment that can presently be endorsed for acute VM are anti-vertiginous and anti-emetic medication.

Prevention

Despite the relative lack of controlled studies demonstrating benefit, many recommend that first measures to treat VM include avoidance of dietary and behavioral triggers, and sleep hygiene.[22] 15% of patients with VM in a recent retrospective study noted symptomatic improvement with caffeine cessation alone, although relief for most was not complete and pharmacotherapy was often prescribed.[24]

Despite a paucity of controlled studies, prophylactic pharmacotherapy can benefit patients with VM who do not have relief after dietary and lifestyle modification.[22] In the previously cited retrospective study, 75% of patients with VM received sufficient relief from caffeine cessation and nortriptyline or topiramate to not proceed to other treatments. In the study, nortriptyline gave relief in 46%, while topiramate gave relief in 25%.[24] In one prospective study of VM, topiramate (50 - 100mg/day) reduced severity and frequency of vertigo and headache attacks.[25]

The American Headache Society - American Academy of Neurology lists Divalproex, Metoprolol, Petasites (butterbur), Propranolol, Timolol and Topiramate as 'established as effective' preventive drugs for episodic migraine.[26] Although, with the exception of Topiramate, the effectiveness of these drugs has not been evaluated in VM

13

it seems reasonable to try them in patients suffering from VM. Other drugs that have been popular in the treatment of VM, such as Amitriptyline (listed as 'probably effective') and Calcium channel blockers (listed as having 'insufficient data to support or refute use') currently enjoy less favor as treatments for chronic migraine.

Physiotherapy for VM may help with complications of VM, such as anxiety, visual dependence or loss of confidence but is not likely beneficial for acute intermittent vertigo attacks.[22]

Opinion on the role, long considered unnecessary, of preventive drug therapy for BPV of childhood seems to be changing. Some now recommend initiating preventive medication if attacks are >2 per month. However, clinical studies are sparse. Specific medications that have been used include topiramate, which can prevent attacks of basilar-type migraine in children and, by inference, may be helpful in VM. Other medications that have been recommended include propranolol, metoprolol, valproic acid, amitriptyline, and flunarizine. Formal data on the effectiveness of these drugs specifically in children is lacking or weak. One large pediatric dizziness center uses magnesium-aspartate 200 - 600mg per day, but doesn't offer data on its effectiveness. [13]

Conclusions

By whatever name, VM remains a nosologic and treatment challenge despite the fact that it affects people of all ages and races. Increasing acceptance of the condition as an independent diagnosis by neurologists and neurotologists leads to hope of better recognition of the many patients who suffer from it and development of evidence-based

14

treatment. For now, suggested treatment is probably best described as: dietary/lifestyle modification, anti-emetic and anti-vertigo medications for acute attacks, and consideration of prophylactic medication usually used to treat chronic or frequently recurrent migraine for patients who find the frequency or intensity of their dizziness/ vertigo sufficiently impairing or disabling. The phenomenon of 'vertigo-associated migraine' should lead the prudent clinician to continually reassess patients with VM since symptoms initially thought due solely to migraine may eventually be shown to be caused by undiagnosed or latent BPPV or Ménière's syndrome.

KEY POINTS

- Vestibular migraine (VM) is under-diagnosed and under-treated because of its varied presentation, lack of biomarkers and lack of officially-accepted diagnostic criteria but is increasingly accepted as a cause of significant morbidity.
- While VM is most commonly a disorder of mid-life that preferentially affects females, VM can occur in patients of both sexes at any age.
- VM and Ménière's syndrome often occur in the same patient and it may not be clear if Ménière's syndrome evolves from migraine or Ménière's attacks (occurring before the development of hearing loss) trigger the migraine features.
- Despite few controlled studies, prophylactic pharmacotherapy with medications such as topiramate may benefit patients with VM who suffer frequent disruptive symptoms even after dietary and lifestyle modification.
- Because vertigo initially thought due to VM may eventually be found to be caused by latent vestibular end-organ disease, regular monitoring of VM patients is warranted.

CITATIONS

1 Cherchi M, Hain TC. Migraine Associated Vertigo. Otolaryngol Clin N Am 2011; 44.367-75

**2 Cherian N. Vertigo as a Migraine Phenomenon. Curr Neurol Neurosci Rep 2013;13:343-8. *Significance: Current summary of the complexity of diagnosis and treatment of VM.*

3 Bisdorff A, Von Brevern M, Lempert T, *et al.* Classification of vestibular symptoms: towards an international classification of vestibular disorders. J Vestib Res 2009;19:1-13.

4 Headache Classification Subcommittee of the International Headache Society. The international classification of headache disorders: 2nd edition. Cephalgia 2004;24:9-160.

5 Radtke A, Neuheuser H, Von Brevern M, Hottenrott T, Lempert T. Vestibular migraine: validity of clinical diagnostic criteria. Cephalalgia 2011; 31:906-13.

6 Eggers SDZ, Staab JP, Neff BA, *et al.* Investigation of the coherence of definite and probable vestibular migraine as distinct clinical entities. Otol Neurotol 2011;32:1144-51.

7 Ruckenstein MJ, Staab JP. Chronic subjective dizziness: Otolaryngol Clin N Am 2009; 42:71-7.

**8 Neff BA, Staab JP, Eggers SD, *et al.*, Auditory and vestibular symptoms and chronic subjective dizziness in patients with Ménière's disease, vestibular migraine, and Ménière's disease with concomitant vestibular migraine. Otol Neurotol

2012;33:1235-44. *Significance: The largest review of Ménière's disease concomitant with VM, highlighting the overlap of the 2 conditions.*

9 Strupp M, Versino M, Brandt T. Vestibular migraine. Handb Clin Neurol 2010;97:755**e**71.

10 Kayan A, Hood JD. Neuro-otological manifestations of migraine. Brain 1984; 107:1123 -42.

11 Battista RA. Audiometric findings of patients with migraine-associated dizziness. Otol Neurotol 2004;25:987-92.

**12 Radtke A, Von Brevern M, Neuheuser H, Hottenrott T, Lempert T. Vestibular Migraine: Long-term follow-up of clinical symptoms and vestibulo-cochlear findings. Neurology 2012; 79:1607-14. *Significance: Highlights the persistent morbidity of VM over a long observation period and suggests that central-type positional nystagmus may help distinguish VM from Ménière's syndrome.*

13 Jahn K. Vertigo and balance in children - Diagnostic approach and insights from imaging. Eur J Ped Neuro 2011;15:289-94.

14 Furman JM, Marcus DA. Migraine and motion sensitivity. Continuum Lifelong Learning Neurol 2012;18(5):1102–17.

15 Bahmad Jr F, DePalma SR, Merchant SM, *et al*. Locus for familial migrainous vertigo disease maps to chromosome 5q35. Ann Oto Rhinol Laryngol 2009;118:670-6.

**16 Murdin L, Davies RA, Bronstein AM. Vertigo as a migraine trigger. Neurology 2009;25:638-42. *Significance: Although 4 years old, this RCT demonstrated the possible mechanism by which peripheral vestibular conditions could trigger migraine symptoms in migraineurs who underwent caloric labyrinthine stimulation.*

17

17 Wise SR, Sargent EW. Migraine as an independent predictor of outcome following endolymphatic sac decompression for Ménière's disease. Poster A274. 116th Annual Meeting at COSM, April 10 - 14, 2013. Orlando, FL.

18 Agarwal K, Bronstein AM, Faldon ME, *et al.* Visual dependence and BPPV. J Neurol 2011;259:1117-24.

19 Polensek SH, Tusa RJ. Nystagmus during Attacks of Vestibular Migraine: An Aid in Diagnosis. Audiol Neurotol 2010;15:241–246.

20 Absinta M, Rocca MA, Colombo B, *et al.* Patients with migraine do not have MRI-visible cortical lesions. J Neurol 2012;259:2695-2698.

21 Hong SM, Kim SK, Park CH, *et al.* Vestibular-evoked myogenic potentials in migrainous vertigo. Otolaryngol Head Neck Surg 2011;144:284-7.

22 Bisdorff AR. Management of vestibular migraine. Ther Adv Neurol Dis 2011;4:183-191.

23 Neuheuser H, Radtke A, von Brevern M, *et al.* Zolmitriptan for treatment of migrainous vertigo. A pilot randomized placebo controlled trial. Neurology 2003;60:882-3.

*24 Mikulec AA, Faraji F, Kinsella LJ. Evaluation of the efficacy of caffeine cessation, nortrpityline, and topiramate therapy in vestibular migraine and complex dizziness of unknown etiology. Am J Otolaryngol 2012;33:121-7. *Significance: Although a retrospective case review that includes patients with poorly defined 'chronic dizziness or undetermined etiology', this current article offers a reasonable approach to the treatment of patients thought to have vestibular migraine.*

25 Gode S, Celebisoy N, Kirazli T, Akyuz A, Bilgen C, Karapolat H, *et al*. Clinical assessment of topiramate therapy in patients with migrainous vertigo. Headache 2010;50:77-84.

**26 Loder E, Burch R, Rizzoli P. The 2012 AHS/AAN guidelines for prevention of episodic migraine: A summary and comparison with other recent clinical practice guidelines. Headache. 2012;52:930-945. *Significance: An essential reference for clinicians considering the use of migraine preventive medication in their patients with VM.*