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HEADACHE (RB HALKER, SECTION EDITOR)

Migraine and Vertigo

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Abstract Vertigo and migraine are commonly co-occurring problems. The diagnostic criteria for vestibular migraine have recently been updated in the International Classification of Headache Disorders, 3rd edition (beta version), which allow better detection of this under-recognized condition. In many cases, a diagnosis of vestibular migraine will be established based on a typical history of concurrent migraine headache, photophobia, and/or migraine aura with the vertigo. Certain mimickers, such as Ménière's disease, likely exist on a pathophysiologic continuum with vestibular migraine. In our review, we provide an update on the salient literature regarding the diagnosis and management of this condition.

Keywords Migraine · Vertigo · Headache · Dizziness · Vestibular

Introduction

Migraine is common, affecting up to 12 % of the population [1]. The disorder is characterized by recurrent, severe headaches often associated with nausea and environmental sensitivities to bright lights and sounds. About 25 % of patients may experience associated transient neurologic symptoms called aura which could manifest as sensory, language, and/or visual phenomena [2]. 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]. Vestibular migraine refers to vertigo that accompanies migraine headache and migraine-associated symptoms (e.g., photophobia and/or aura), which has also been referred to as migraine-associated vertigo/dizziness, migraine-related vestibulopathy, and migrainous vertigo. In childhood, a history of motion sickness is associated with the later development of migraine, and vestibular activation attenuates migrainous symptoms, all indicating shared neurobiologic elements [4, 5]. As will be discussed, Ménière's disease, migraine with brainstem aura, and benign positional vertigo of childhood are other conditions that are included in the spectrum of migraine with associated vertigo.

The epidemiology of migraines has been studied in great detail but, the epidemiology of migraine and vertigo coexistence, less so. While dizziness, vertigo, and migraine are all common in the population, vestibular migraine has been estimated to only occur in 1–3 % of individuals [6]. This data is subject to under-reporting given recent consensus of criteria for vestibular migraine in the recent years only [7].

When faced with a patient presenting with both migraine and vertigo, it can be clinically challenging to establish what the primary pathology is which should be treated. Disease-related and experimentally induced vertigo have both been postulated to trigger migraine headaches. In a provocative study of 39 participants with a history of migraine that underwent caloric testing, 19 (48 % of patients) experienced their usual migraine within 24 h, as compared to only 1 of 21 (5 %) from the matched control group [8]. These findings serve to highlight vestibular activation as a relatively potent migraine trigger. These interactions may stem from known intrinsic connectivity between trigeminal afferents and vestibular nuclei in the brainstem [9]. Along these lines, supraorbital nerve stimulation has been noted to evoke or modify nystagmus in eight out of ten (80 %) patients with migraine in one study [10].

Given the overlap in symptoms and likely shared pathophysiology between multiple syndromes (e.g., vestibular migraine and Ménière's disease), there is often diagnostic

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confusion among patients and providers, alike. Work in this field has been hampered by difficulty in establishing diagnostic criteria and disagreement among varying subspecialists. The recent recognition of vestibular migraine in the International Classification of Headache Disorders, 3rd edition (beta version) (ICHD-3), represents an important step towards the systematic study of this disorder, despite only appearing in the appendix section [11••]. In this review, we will expand upon contemporary thinking regarding migrainous vertigo, the most salient differential diagnosis, and management considerations in this patient subpopulation.

Pathophysiologic Considerations

The pathophysiology of migraine is incompletely understood. In general, migraine is a heterogeneous, genetic disorder of the brain, characterized by a failure of cortical habituation in electrophysiological testing [12–14]. The so-called vascular hypothesis of migraine is increasingly falling out of favor [15, 16]. Cortical spreading depression is the likely pathophysiologic substrate of aura symptoms. Vestibular symptoms in migraine are of uncertain etiology. They may represent brainstem aura phenomena or could result from cortical spreading depression in the parietal lobes influencing the vestibular nuclei in the brainstem through direct cortical projections [17]. Magnetic resonance imaging (MRI) determined volumes of temporal lobes, dorsolateral prefrontal cortices, and insular lobes that have been observed to be negatively correlated with headache severity and duration of symptoms in patients with vestibular migraine suggesting that alterations identified in vestibular migraine extend to areas involved in multisensory vestibular control and central vestibular compensation, possibly representing the pathoanatomic connection between migraine and the vestibular system [18]. In patients with vestibular migraine undergoing cold-water ear irrigation, brain oxygen level-dependent (BOLD) functional MRI showed statistically significant thalamic activation as compared to healthy controls which correlated positively with frequency of migraine attacks [19]. ^{18}Flurodeoxyglucose positron emission tomography scans of vestibular migraine patients during attacks showed significantly increased metabolic activity in insular and thalamic regions suggesting activation of the vestibular-thalamic-cortical pathway [20].

Channelopathies are another proposed mechanism for both migraines and vertigo. This hypothesis is supported by the finding of a calcium channel abnormality encoded in CACN A1A on chromosome 19p that may manifest with either episodic ataxia type 2 or familial hemiplegic migraine type 1 [21]. Other channelopathies manifested with ataxia, vertigo, and at times, migraine have also been described [22].

Vestibulopathy has been proposed as another mechanism of production of migraines and vertigo. Damage to the vestibular and inner ear apparatus has been reported in a large number of patients with migraines with and without vertiginous symptoms. Endolymphatic hydrops is a proposed cause of Ménière's disease and related conditions like benign paroxysmal positional vertigo (BPPV) [23]. Many patients with BPPV and Ménière's disease report having headaches with migrainous features in addition to their vertigo. Many experts believe that migraines, vertigo, BPPV, and Ménière's disease are all related conditions along the spectrum of the same process differing only in severity of symptoms. Frequent coexistence of these conditions and related symptoms has lent credence to this school of thought.

Vestibular Migraine

Vertigo may occur during or in between headache episodes, where it may be associated with non-headache migraine symptoms, such as photophobia or visual aura. The duration of vertigo in vestibular migraine is highly variable, lasting on the order of minutes to days [24]. It is the unpredictable and intermittent nature of these symptoms that has led to differences in terminology and descriptions for what is essentially believed to be a very closely related group of disorders.

The Neuheuser diagnostic criteria have been previously used to classify patients as having definite or probable vestibular migraine [25]. Probable vestibular migraine has been thought to represent a heterogeneous group, where the relationship between migraine and vertigo symptoms may not be as clear, and some patients may also meet criteria for Ménière's disease [26]. More recently, vestibular migraine has been defined in the appendix of the ICHD-3 (Table 1), which should be considered as the gold standard for prospective research studies on this topic. Allowance of prior

Table 1 ICHD-3 beta version appendix criteria for diagnosis of vestibular migraine

A. At least 5 episodes fulfilling criteria C and D

B. A current or past history of migraine with or without aura

C. Vestibular symptoms of moderate or severe intensity, lasting between 5 min and 72 h

D. At least 50 % of episodes are associated with at least 1 of the following 3 migrainous features:

  a. Headache with at least 2/4 characteristics
    - Unilateral
    - Pulsating quality
    - Moderate or severe intensity
    - Aggravation by routine physical activity
  b. Photophobia and phonophobia
  c. Visual aura

E. Not better accounted for by another ICHD-3 diagnosis or by another vestibular disorder

considerations such as response of vertigo to migraine medications and precipitation by food triggers, sleep irregularities, and hormonal changes has been eliminated in the ICHD-3.

The evaluation of vestibular migraine consists of a detailed history of both the headache and vestibular components, in addition to potential testing, such as imaging and audiometry. There are no pathognomonic abnormalities on neuroimaging or audiovestibular testing. The concurrent presence of migraine headache, environmental sensitivities, and/or visual aura with vertigo should be ascertained as these features would allow application of ICHD-3 diagnostic criteria for vestibular migraine. The presence of hearing loss, especially if significant and asymmetric, may indicate inner ear pathology such as Ménière's disease (Fig. 1).

Testing may include caloric testing and pure tone audiometry to assess baseline inner ear function. Dedicated computed tomography (CT) of the temporal bone may help diagnose mimickers such as superior canal dehiscence, where symptoms can include sound-induced vertigo (Tullio phenomenon) and autophony, where self-generated noises become amplified, such as during breathing and even eye movements. Dedicated MRI with thin slices through the pontomedullary junction may be informative when audiovestibular testing indicates a potential central lesion. Noninvasive angiography should be considered if there is concern for vertebrobasilar insufficiency producing vertiginous symptoms. Pure tone audiometry is useful because it acts as an objective test of hearing damage, which may be used as part of the diagnostic criteria for Ménière's disease, where low-frequency hearing loss is often seen (Table 2). Hearing loss may also be seen in patients with vestibular migraine; however, this is most often bilateral and not severe [27•]. In contrast, patients with Ménière's disease often have asymmetric hearing loss of a more profound magnitude. Electrophysiologic studies like brainstem-evoked response audiometry or electronystagmography are less useful in diagnosis due to their sensitivity in picking up mild dysfunction in many normal people as well as nonspecific abnormalities [24].

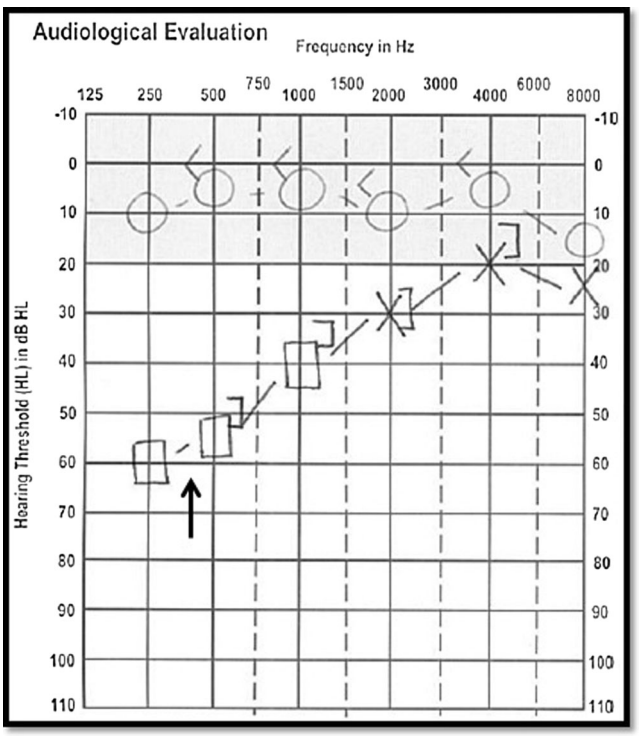

Fig. 1 Audiogram in a patient with Ménière's disease showing low-frequency sensorineural hearing loss in the left ear (*arrow*). Audiogram courtesy of Dr. Matthew L. Bush, Department of Otolaryngology-Head and Neck Surgery, University of Kentucky

Treatment involves a multidisciplinary approach to ensure maximum benefit to the patient but is based on the very limited body of literature. Abortive therapy using anti-migraine medications like triptans and antiemetics such as promethazine and meclizine has been thought to be helpful [28, 29]. Prophylactic therapy involves using anti-migraine medications with anecdotal preference for verapamil, topiramate, and lamotrigine [29, 30]. A recent study showed significantly increased benefit in the treatment of vertigo in vestibular migraine patients using flunarizine in addition to betahistine, a finding that supports the role of calcium channel dysregulation in the pathogenesis of vestibular migraine [31]. Avoidance of triggers may be useful in preventing attacks. Vestibular therapy may be beneficial to patients, especially if they have comorbid chronic subjective dizziness (see below) [32]. Patients with suspected episodic ataxia may benefit from treatment with acetazolamide [33]. Other treatment modalities include treatments for the comorbid conditions like Ménière's disease, BPPV, generalized anxiety disorder, and chronic subjective dizziness to minimize discomfort and provide optimal quality of life and symptomatic relief.

The prognosis for vestibular migraine is not well understood. In a study involving 61 patients, 87 % of patients complained of significantly persistent vertigo affecting their quality of life over a follow-up period of 9 years. About 45 % of patients said that their vertigo had neither changed nor worsened during this period, while nearly 64 % said that their vertigo was moderately or severely disabling during their daily activities. Concomitant symptoms of hearing loss with vertigo had increased from 15 to 49 % of patients over this duration. Interestingly, seven out of 61 (11 %) patients with an initial diagnosis of vestibular migraine developed low-frequency hearing loss over a median follow-up of 9 years

Table 2 Diagnostic criteria for definite Ménière's disease

Two spontaneous episodes of rotational vertigo lasting at least 20 min
Audiometric confirmation of sensorineural hearing loss
Tinnitus and/or a perception of aural fullness
Exclusion of other known causes of symptoms

sufficient to allow diagnosis of Ménière's disease [27•]. Therefore, patients with vestibular migraine should be counseled of the probable pathophysiologic continuum with Ménière's disease and be referred for audiogram testing as clinically indicated.

Assessing for Comorbidity

Ménière's disease is a frequent comorbidity with vestibular migraine. The relationship between the two disorders is complex, as there is a significant overlap of symptoms and there are likely shared pathophysiologic mechanisms. Nearly 60 % of patients with Ménière's disease will have comorbid migraine, where criteria for vestibular migraine will often also be met [34]. Patients with vestibular migraines and other comorbid conditions are more likely to have worse quality of life measures as compared to those without the comorbidities, a factor that is always taken into consideration during treatment [26].

BPPV is another frequently associated comorbidity with vestibular migraine [35]. Such an overlap between the incidence of BPPV, Ménière's disease, and vestibular migraine symptoms has prompted many experts to suggest that these conditions are all part of the same spectrum of cochleovestibular dysfunction disorders [35].

Chronic subjective dizziness (CSD) is another entity in the spectrum of migraine and vestibular disorders. Diagnostic criteria include (1) persistent nonvertiginous dizziness lasting 3 months or more; (2) hypersensitivity to motion stimuli, including a patient's own motion or motion of objects in the visual environment; and (3) aggravation of symptoms with precision visual tasks, such as reading or computer use [36•]. Vertigo is not a part of CSD but is a common comorbidity. Symptoms tend to be maximal with upright posture (but are not orthostatic) and in visually provocative settings, such as a shopping mall. The syndrome may be triggered by an initial vestibular event, such as BPPV or vestibular neuritis. Behavioral assessment of these patients may reveal psychological stressors and comorbid generalized anxiety and/or panic disorder. Physical examination and testing may reveal some neuro-otologic abnormalities, but these are usually nonspecific. The exact cause of CSD is unknown, but current hypotheses in the field include operant and classic conditioning versus failure of readaptation of vestibular mechanisms as the primary pathophysiologic mechanisms. Treatment options include selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors, in addition to vestibular and balance rehabilitation therapy [36•].

Vertigo is known to be an inherently anxiety-provoking experience, and patients may develop an incident generalized anxiety and/or panic disorder following an initiating vestibular event. Even further, patients not uncommonly experience aggravation of preexisting generalized anxiety disorder following the onset of disorders characterized by vertigo [37]. This is an important observation, as generalized anxiety disorder and panic disorder are among the most strongly linked migraine comorbidities identified. Finally, concurrent health-related anxiety, previously known as hypochondriasis, may be an important component to address to optimize treatment outcomes [38].

Differential Diagnosis

In considering the differential diagnosis for vestibular migraine, one should recall the diagnostic caveat that vestibular activation can commonly secondarily provoke migraine attacks.

The differential diagnoses would include conditions that could produce vertigo and headaches. Ménière's disease, BPPV, vertebrobasilar insufficiency, vestibular neuronitis, inner ear damage from trauma or infection, otitis media, acoustic neuromas, and other cerebellopontine angle lesions in addition to brainstem lesions are all in the differential for vertigo with varying degrees of headache. Migraine with brainstem aura is a frequently encountered differential for migraine with vertigo but can be differentiated from vestibular migraine by the presence of other bulbar features, such as diplopia. Posttraumatic headache and vertigo may be due to posttraumatic headache, vertebral artery dissection, superior canal dehiscence, and posttraumatic BPPV. Episodic ataxia type 2 is another uncommon condition to be considered in the differential given the nature of presenting symptoms and their overlap with vertiginous conditions. While typically thought of as a genetic disorder arising in childhood, sporadic acetazolamide-responsive cases have been observed in adults with relatively long-duration (hours to days) attacks of headache, vertigo, and ataxia. Otherwise, unexplained vermian cerebellar atrophy may be seen on MRI.

Many of these conditions can be screened for with careful history and neuro-otologic examination.

Conclusions

Migraine headaches and vertigo are common complaints at presentation in many outpatient neurology clinics. Clinicians should be aware that vestibular migraine is likely underrecognized and that migraine headache may be a secondary phenomenon triggered by an underlying vestibular disorder. In many cases, a diagnosis of vestibular migraine will be established based on a typical history of concurrent migraine headache, photophobia, and/or migraine aura with the vertigo. Careful history taking, physical examination, and testing are utilized to rule out secondary causes. Certain mimickers, such

as Ménière's disease, may actually exist on a pathophysiologic continuum with vestibular migraine. Symptomatic and prophylactic migraine therapy can be used in conjunction to manage vestibular migraine in many cases.

Compliance with Ethics Guidelines

Conflict of Interest Arun Swaminathan and Jonathan H. Smith declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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