

CASE REPORT

Case reports on two patients with episodic vertigo, fluctuating hearing loss and migraine responding to prophylactic drugs for migraine. Menière's disease or migraine-associated vertigo?

Caso clinico di due pazienti con episodi di vertigine recidivante, ipoacusia fluttuante ed emicrania con buona responsività alla terapia profilattica per l'emicrania. Malattia di Menière o vertigine emicranica?

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SUMMARY

Recent reports have focused on a possible association between migraine and Menière's disease; patients suffering from Menière's disease present a higher rate of migraine. In some cases, the clinical features of migraine-associated vertigo may mimic the presentation of Menière's disease. The present report focuses on two cases of females with recurrent episodes of rotational vertigo, fluctuating hearing loss and tinnitus lasting from a few minutes to several hours; both cases also presented migrainous attacks. As a result of repeated cochleovestibular attacks, both patients presented a permanent low frequency sensorineural hearing loss. Preventive therapies for Menière's disease did not reduce vertigo attacks, while topiramate and acetylsalicylic acid treatment resulted in a significant reduction of both migraine and vertigo. Both the diagnosis of Menière's disease and of migraine-associated vertigo rely on clinical history and both disorders lack a specific diagnostic test. In the early stages, differential diagnosis between Menière's disease and migraine-associated vertigo is often very difficult; previous investigations focused on the possibility that subjects with migraine may experience all symptoms of Menière's disease, including sensorineural fluctuating hearing loss. In conclusion, a trial with prophylactic drug treatment for migraine might be suggested in patients with clear symptoms of migraine and recurrent cochleovestibular disorders.

KEY WORDS: Vertigo • Menière's disease • Migraine • Migraine-associated vertigo • Sensorineural hearing loss

RIASSUNTO

Recentemente la letteratura scientifica ha posto l'attenzione sulla possibile associazione tra emicrania e malattia di Menière; pazienti affetti da malattia di Menière presentano una più alta incidenza di emicrania. In alcuni casi, le manifestazioni cliniche della vertigine emicranica possono mimare la presentazione della malattia di Menière. Presentiamo due casi di pazienti donne con episodi ricorrenti di vertigine rotazionale, ipoacusia fluttuante e acufene della durata variabile da minuti ad ore; entrambi i casi presentavano attacchi di emicrania. Come risultato di reiterati attacchi cocleovestibolari, i pazienti presentavano ipoacusia neurosensoriale permanente per le basse frequenze. La terapia di prevenzione per la malattia di Menière non riduceva gli attacchi vertiginosi, mentre la somministrazione di topiramato e acido acetilsalicilico determinava una drastica riduzione sia dell'emicrania sia della vertigine. Entrambe le diagnosi di malattia di Menière e vertigine emicranica si basano sulla storia clinica e non posseggono test diagnostici specifici. Negli stadi precoci, la diagnosi di differenziale tra malattia di Menière e vertigine emicranica è spesso piuttosto difficoltosa; lavori precedenti sottolineano la possibilità che soggetti affetti da emicrania possono manifestare tutti i sintomi di malattia di Menière, inclusa l'ipoacusia neurosensoriale fluttuante. In conclusione, una terapia farmacologica profilattica per emicrania potrebbe essere consigliata nei soggetti con franca sintomatologia emicranica associata a disordini cocleovestibolari ricorrenti.

PAROLE CHIAVE: Vertigine • Malattia di Menière • Emicrania • Vertigine emicranica • Ipoacusia percettiva

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Introduction

Menière's disease (MD) is an inner ear disorder characterized by recurrent episodes of rotational vertigo, most typically associated with fluctuating progressive hearing loss, typically on low frequencies in early stages, fullness and tinnitus. Raised endolymphatic pressure (hydrops) is commonly accepted as the causal condition^{1,2}.

Criteria used to define MD are: the presence of at least two episodes of vertigo of at least 20 minutes' duration, audiometrically confirmed sensorineural hearing loss on at least one occasion, tinnitus or aural fullness during episodes and exclusion of other possible causes of vertigo³. Prosper Menière himself observed the association between MD and migraine⁴.

Various studies have focused on the higher prevalence of migraine in MD patients, variously reported at between 43% and 56%, while in the normal population it is 10%^{5,6}.

On the other hand, there is a higher prevalence of MD in a population screened for migraine compared to the incidence in the general population⁷. Epidemiology of both MD and migraine-associated vertigo (MAV) may underline a possible pathogenetic link between the 2 diseases^{8,9}.

Migraine is an increasingly recognized cause of recurrent vestibular symptoms; features of MAV include both true rotational vertigo and subjective vertigo lasting from a few minutes to days. During attack-free periods, several studies have documented vestibular anomalies in 30-55% of subjects¹⁰⁻¹².

According to Neuhauser et al.¹³, diagnostic criteria for definite MAV are:

- episodic vestibular symptoms of at least moderate severity (rotational vertigo, other illusory self or object motion, positional vertigo, head motion intolerance);
- at least two of the following migrainous symptoms during at least two vertiginous attacks: (a) migrainous headache, (b) photophobia, (c) phonophobia, (d) visual or other auras;
- attacks of migraine (independently of episodes of vertigo) according to International Headache Society (IHS) criteria;
- some central and/or peripheral vestibular abnormalities found in vertigo-free periods.

MAV is the main disorder capable of mimicking MD in its early stages. There is clinical evidence that migraine can damage the inner ear, causing permanent hearing loss or impairment of vestibular function^{14,15}. Some authors have hypothesized that MD may develop in an ear previously damaged by vasospasm induced by migrainous mechanisms¹⁶.

The present report refers to two migrainous patients, presenting with repeated episodes of rotational vertigo with permanent sensorineural hearing loss fulfilling all of the criteria for definite MD; their response to treatment for MD was poor whilst they showed a satisfactory response to prophylactic drugs for migraine.

Case reports

Case 1

This patient, a 42-year-old female, was suffering from migraine with aura according to IHS criteria. The final diagnosis was made by a senior neurologist. The patient reported the first attack of migraine at the age of 20 years, which more typically occurred before menstruation, at a frequency of 1-2/month. Her family history was positive for migraine (mother and one of three sisters). Blood tests showed repeated positivity for lupus-like anti-coag-

ulants; anti-nuclear, anti-mitochondria, anti-thyroid, anti-cardiolipin auto-antibodies and rheumatoid factor, on the other hand, resulted negative. She also presented normal C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), serum protein electrophoresis, a normal aPTT and normal C3 and C4 levels. Central nervous system nuclear magnetic resonance (NMR) imaging demonstrated micro-ischaemic lesions. High resolution computerized tomography (CT) scan was normal. She was not receiving any pharmaceutical treatment for migraine at the time of our evaluation.

In the previous 2 years, the patient reported recurrent episodes of rotational vertigo (about 1/month) lasting from a few minutes to 1-2 hours, often with a right ear fluctuating hearing loss. Migraine and vertigo never occurred together. As a final result, her audiometric threshold showed a right sided low frequency sensorineural hearing loss. Pure tone audiometry (PTA) average at 250-500 and 1000 Hz was 35 db, while PTA average at 1-2 and 3 KHz was 15 db. She also reported the presence of tinnitus which increased before vertigo attacks. Acoustic evoked potentials were normal. As a result of the short duration of vertigo, we were unable to perform an audiometric examination during vertigo attacks. Her left ear showed a normal threshold. Caloric tests demonstrated a right sided unilateral weakness (26%) during caloric stimulation according to Freyss and the Head Impulse Test was positive on the horizontal plane with refixation saccades towards the left side. Vestibular evoked myogenic potentials (VEMPs) were also recorded with an ipsilateral technique, using a short broadband click of 0.1 msec duration, while the subject was seated upright with her chin turned towards the contralateral shoulder. Ongoing EMG activity was visually monitored on an oscilloscope to ensure tension on the sternocleidomastoid muscle greater than 65 μ V during recording. The patient presented normal bilateral broadband click-evoked cervical VEMPs for latency and amplitude; on the other hand, she presented a normal 120 db SPS (Sound Pressure Level) threshold on the unaffected side but a 10 db threshold shift on the right side.

Case 2

This patient, a 59-year-old female with a long history of migraine which began at the age of 23 and ceased at the age of 50, immediately after onset of menopause. She had normal blood tests (above all rheumatologic tests), normal central nervous system NMR imaging and normal high resolution inner ear CT scan. Over the last year, she reported various episodes of rotational vertigo normally lasting for 2-3 hours with hearing loss on the left side. She reported increased hearing loss during vertigo. Audiometric examinations demonstrated a low frequency sensorineural hearing loss (PTA at 250-500 and 1000 HZ 30 db while PTA at 1-2 and 3 KHz 20 db); acoustic-evoked potentials presented normal latencies. Caloric tests

according to Freyss demonstrated a unilateral weakness of 40%; Head Impulse Test was positive with corrective saccades towards the right side on the horizontal plane.

Cervical VEMPs were normal for latency, amplitude and threshold.

The two patients fulfilled all AAOHNS criteria for definite MD. In both cases, preventive therapy of MD with betahistine 24 mg twice a day, salt restriction and increased water intake did not prevent vertigo attacks, which remained unchanged in frequency and duration in a 6-month follow-up. On the other hand, drug prophylaxis of migraine with topiramate 100 mg a day and disaggregants (acetylsalicylic acid 100 mg a day) produced a clear decrease in vertigo attacks, in both patients, in a 1-year follow-up, since patient 1 did not report any episodes of vertigo and patient 2 reported only one mild episode of about 10 min. Patient 1 also reported a reduction in migraine attacks since she reported only one mild episode. Dietary changes, to reduce the triggers for migraine (above all caffeine, chocolate and red wine), were suggested to both patients.

In both cases, the audiometric thresholds remained constant.

Discussion

The signs and symptoms of MAV sometimes show an overlap with those of MD; in these cases, differential diagnosis is often difficult. Both MD and MAV diagnoses rely considerably on history and both disorders lack a definite diagnostic test. It should be noted that, at present, "hearing is the most readily measured variable and the variable most related to the natural history of Menière's disease"³.

Previous investigations have focused on case studies in which differentiating between the two disorders is a puzzling dilemma¹⁷.

Vestibular anomalies, such as spontaneous or positional nystagmus, failed to offer a reliable test to differentiate the 2 disorders; percentage of asymmetric caloric responses, reported in an average of 24.5% of cases of MAV, magnitude of unilateral weakness and rotational tests have not been reported to be useful in discriminating between the two disorders^{10 18}.

Patients with MAV may experience all the symptoms of MD, including fluctuating sensorineural hearing loss¹⁹, even though repeated MAV attacks very rarely produce a permanent hearing loss²⁰.

A fluctuating hearing loss in children has been considered, by some authors, as a migraine equivalent²¹.

As also in our two patients, the majority of patients with MAV have attacks of dizziness independently of migraine headache; it should be noted that in our second patient, vertigo spells began when migrainous attacks ceased^{22 23}. Topiramate blocks voltage-sensitive sodium channels and voltage-activated calcium channels, inhibits glutamate re-

lease, and increases GABA levels²⁴. Some large studies have demonstrated that topiramate is a safe, effective, and well-tolerated drug for migraine prophylaxis. Above all, few side-effects are described when topiramate is used at doses up to 100 mg a day^{25 26}.

These cases underline that there are some doubts concerning the statement that "fluctuating hearing loss with vertigo is almost always due to Menière's disease", moreover the pathophysiological conditions of MD and MAV are poorly understood^{4 27}.

Some further considerations should be added regarding lupus anti-coagulant (LAC) positivity, white matter micro-ischaemic lesions and migraine. LAC positivity, as well as the presence in blood of anti-cardiolipin and β_2 -glycoprotein I antibodies, is widely known as the antiphospholipid syndrome; the main characteristic of the disease is an antibody-mediated hypercoagulable state characterized by recurrent venous and arterial thromboembolic events. Primary antiphospholipid syndrome refers to patients who do not have any other rheumatologic or autoimmune conditions, whereas secondary antiphospholipid syndrome refers to patients who also have systemic lupus erythematosus (SLE) or other conditions. In general, the clinical manifestations of the antiphospholipid syndrome are similar for primary and secondary forms of the disease²⁸. Antiphospholipid antibodies are found among young, apparently healthy control subjects at a prevalence of 1 to 5%. Cerebro-vascular events have been reported to be positively associated with the antiphospholipid syndrome^{29 30}. An association between Behcet's Disease and cerebral blood flow perfusion impairment has been demonstrated with a SPECT examination even in subjects with normal MRI findings³¹. A possible role of antiphospholipid antibodies, in the pathogenesis of migraine, is still under debate. No association has been found between anti-cardiolipin autoantibodies and migraine in a paediatric population³², while in adults, with some exceptions³³, the prevalence of migraine, above all with aura, has been reported to be higher in SLE subjects than in the normal population³⁴⁻³⁸, and an association with antiphospholipid syndrome has been suggested³⁹. The American College of Rheumatology included headache and migraine among the neuro-psychiatric syndromes observed in SLE⁴⁰.

More frequently, in autoimmune disorders, neurologic involvement is reported to be present in between 4 and 49%, and, moreover, in 5% of cases, it is the initial feature; immuno-mediated disease activity may justify the higher prevalence of migraine in autoimmune disorders and the cerebral MRI findings^{41 42}.

The overlapping signs and symptoms between MD and MAV have caused some Authors to suggest the possibility of a common link in the pathogenesis of the two diseases.

As the vestibular nuclei receive noradrenergic fibres from the *locus coeruleus*⁴³ and serotonergic afference from the

dorsal raphe nucleus⁴⁴, it is likely that activation of these pathways, in migraine, could also activate central vestibular processing⁴⁵. Moreover, the reciprocal connection of vestibular nuclei and trigeminal nucleus *caudalis* may provide a close link between vestibular and vascular-trigeminal processing during migraine attacks and trigeminal inner ear sensory innervation may explain the peripheral neuro-otological disorders. Short duration vertigo may be related to vasospasm-induced ischaemia of the labyrinth and repeated episodes may lead to irreversible damage⁴⁶. Moreover, it has been suggested that endo-lymphatic hydrops may develop in an ear previously compromised by vasospasm due to a migrainous mechanism¹⁴.

Shepard¹⁷ suggested the following practical criteria in order to differentiate MD and MAV:

- The use of a consistent and verifiable definition of MAV is important for consistency and comparison across facilities and clinical trials regarding diagnoses

and treatment. MAV must be considered as part of the differential diagnosis.

- In the patient's history, the report of only very short (seconds to less than 15 minutes) or prolonged (more than 24 hours) vertigo spells are more likely due to migraine rather than MD. Moreover, if the spontaneous spells of vertigo are associated with migraine features (phono- or photo-phobia), migraine is the probable source.
- In MAV, audiometric and vestibular anomalies are more typically mild in magnitude and stable over time rather than fluctuating.

As a final personal consideration, when symptoms coexist with migraine, a trial with a migraine management regimen is suggested. MAV is, above all, a diagnosis of exclusion based on clinical history⁴⁷. It should be of some importance, the idea that aggressive drug treatment for migraine is anyway more mild than aggressive treatment for MD.

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