Recent onset disequilibrium mimicking acute vestibulopathy in early multiple sclerosis

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\section*{ABSTRACT}

The differential diagnosis of patients with acute unilateral vestibulopathy rests in the proper clinical assessment and use of selected tests of vestibular function. In case of a central nervous system lesion as in Multiple Sclerosis, the case shown here, it is of particular importance to observe congruency between severity of symptoms and signs and, of topographic diagnosis. We report a case of a 37 year old woman with recent onset disequilibrium that after careful analysis of the different test results several incongruences were found; this prompted a radiological study that provided the clue to diagnosis. After treatment the patient recovered completely not only clinically but also in vestibular deficit.

\section*{1. Introduction}

The evaluation of patients complaining of disequilibrium needs adequate interplay of the clinical characteristics after a detailed medical history and specific vestibular testing coupled with orientated ancillary methods of neurological function and imaging. The medical history should focus on some clinical issues of symptoms the most relevant of which are the following: their duration (recent onset or chronic), the existence of identifiable vestibular antecedents (acute vestibulopathy, Meniere’s disease, etc), of risk factors for dizziness (neurological, cardiovascular, visual, etc) and, whether there is a disorder during gait or this is only perceived by the patient. A proper bedside vestibular examination is the key step for the selection of following tests [1].

All this has provided increasing awareness of puzzling clinical cases of which most frequently a peripheral vestibulopathy is considered, in accordance with the pattern in their initial symptoms and signs but concludes as a central lesion after complete examination and work up; this is more frequent in stroke [2], but less for multiple sclerosis [3] and vestibular schwannoma [4].

We present a case in where the clinical symptoms and vestibular evaluation found some incongruities.

\section*{2. Case reports}

A 37 year old woman presented to our hospital due to unsteadiness that worsened with ambulation and abrupt head movements, associated with nausea and vomiting. She denied tinnitus, hearing loss or any other otological symptoms; nor was there was a precedent vertigo spell. It had all begun 15 days before visiting the physician and its severity remained constant. The patient stated...
she had fallen twice: while walking down the stairs and while getting up from bed. Subsequently, the patient had difficulty focusing her vision, oscillopsia and right hemifacial numbness.

Three years before, following her first pregnancy she had urinary incontinence for 8 months. A year later, she was seen because of an acute right otitis media. At that time a mixed hearing loss was detected in her right ear and a moderate sensorineural hearing loss in her left ear: the bone conduction audiometry was worst in her right ear. She was treated by myringotomy to evacuate middle ear effusion; 1 month later the tympanic membrane and middle ear were normal as was hearing in both ears: the pure tone average was lower than 10 dB in all the frequencies. Also, the patient had suffered migraines with aura for many years.

At the time of diagnosis in her actual problem otological examination showed normal bilateral otoscopy.

Neuro-otologic examination showed spontaneous left beating nystagmus with an upbeat component under Frenzel glasses in a completely darkened room. In primary position the slow-phase velocity (SPV) of nystagmus was 12°/s for the horizontal component and 5°/s for the vertical component. Both components of nystagmus SPV increased in leftward gaze and almost disappeared in rightward gaze; upward and downward gaze had no effect on any of the components of nystagmus. This nystagmus was seen in all the positions examined (supine, left and right lateral) and increased in velocity after head shaking. Visual fixation effectively suppressed the nystagmus. There was small non-quantified skew deviation on cover test during which the right eye was the lower.

The vestibulo-oculomotor reflex (VOR) was examined with the Video Head Impulse test (vHIT, GN Otometrics). Rightward head thrusts disclosed abnormal results for all the semi-circular canals (SC). This was evident for the vertical canals (superior, SSC and posterior, PSC) with low gains and less for the horizontal (HSC), although clear refixation saccades (covert and overt) were registered. Leftward head thrusts provoked normal responses for all the SC (Fig. 1).

A normal pure-tone audiometry was obtained in both ears. Brainstem auditory evoked potentials (BAEP), applying clicks of 70 dB HL, were normal for both ears.

Vestibular evoked myogenic potentials (VEMP) were done using 0.5 kHz stimulation (airborne) at 95 dB nHL and registering at the ipsilateral SCM: on the right side the rectified response was abnormal (the p13 latency was 16.3 ms and the n23 latency was 22.3 ms with an interpeak amplitude of 5.8 μv) but no response was obtained after left-side stimulation (Fig. 2A). Clear later components (n34 and p44) are obtained after right ear stimulation.

A brain MRI performed showed multiple supratentorial periventricular foci (Fig. 3A). In addition, two infratentorial foci were present (Fig. 3B), one in the right middle cerebellar peduncle and the other in the left cerebellar lobe. After paramagnetic contrast, 2 enhancing lesions were observed, located in the right middle cerebellar peduncle (Fig. 3C) and left frontal lobe (Fig. 3D). Cervical and thoracic spinal cord MRI showed multiple foci of increased signal in the left cervical

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**Fig. 1** – Recording of the VOR after head impulses in the plane of each semicircular canal in both ears at the time of diagnosis. In blue and red, the head velocity profile and in green the eye velocity corresponding to each head impulse; refixation saccades are depicted in black. In the center hexagonal plot of mean gain of the responses: in red, abnormal results, and in green, normal results. LA: left anterior semicircular canal, LL left lateral or horizontal semicircular canal, LP left posterior semicircular canal, RA: right anterior semicircular canal, RL right lateral or horizontal semicircular canal, RP right posterior semicircular canal.
cord (Fig. 3E) without paramagnetic contrast enhancement predominantly. Complementary studies performed were a lumbar tap showing multiple oligoclonal bands in the cerebrospinal fluid (Fig. 3F), an IgG/albumin ratio of 1.3 and the multimodal pattern shift evoked potentials showing delayed latency in the right visual evoked potential.

The diagnosis of multiple sclerosis was established and a steroid treatment was initiated with a significant clinical recovery in follow-up at 1 month. Downbeat nystagmus is registered in primary eye position under Frenzel glasses and increases significantly (without fatigue) in the supine and head hanging position in

Fig. 2 – VEMP recording for right and left ear stimulation. In (A), at the time of diagnosis and in (B), after treatment. In blue is the raw data for the left side, and in black underneath, the rectified response. In red, the same data for the right ear.

Fig. 3 – MRI (brain and spinal cord) and oligoclonal bands (cerebrospinal fluid and blood serum).
which no complete visual suppression is obtained. A normal exam for VOR (Fig. 4) and VEMPs (Fig. 2B) was obtained at the time.

3. Discussion

This case was a dilemma at the time of diagnosis, during initial bedside examination and vestibular testing as some incongruities were found helpful for the diagnosis that we will review.

1. Incongruence between clinical symptoms and vestibular examination. The patient was seen at the regular dizziness clinic because of unsteadiness and postural disorder while vestibular examination was typical of an acute right peripheral vestibulopathy. The intense left-beating spontaneous nystagmus followed Alexander’s law and increased after head shaking, coupled with an abnormal oculomotor response to a rightward head impulse, suggested an acute right, peripheral vestibulopathy. To confirm this suspicion a vHIT was carried out and showed a hypofunctional right vestibulo-ocular reflex: the eye velocity response to the rapid head impulse is lower than normal and left refixation saccades must occur to place the eyes back on the fixation target. In particular, these saccades had a disorganized pattern usually seen in patients with acute or uncompensated chronic unilateral vestibulopathy [5]. The difference between the clinical status and the striking abnormalities in the vestibular examination was very intriguing and usually considered to provide a clue for a central vestibular disorder; however the severity of symptoms at onset is not always related to the size or localization of the vestibular damage [6].

2. The possibility of testing the VOR in a detailed manner, after stimulation of each of the six semicircular canals, is a recent advance at the clinical level [7]. Applied in this patient, it has provided an additional pattern of abnormality in the VOR assessment as the deficit in the vertical canals (SSC and PSC) exceeded the HSC deficit. This pattern is unexpected according to previous published results in patients with acute unilateral peripheral vestibulopathy in which three distinct patterns of semicircular involvement were obtained: 1) loss of HSC function only or of HSC and SSC function, 2) loss of SSC, HSC and PSC function and, 3) loss of only PSC function [8]. These findings respond to the particularities of the innervation of the vestibular periphery as the information from the SSC and HSC travel along the superior branch of the vestibular nerve and that from the PSC through the inferior one. As such, when damage occurs in the labyrinth or in any of the branches of the vestibular nerve a unique combination of deficits is to be expected. In our patient mainly vertical canal damage with modest HSC damage is a combination that raises the suspicion of a central vestibular localization.

3. Nystagmus shows some particularities worthy of mention. The patient was examined in an enclosure to maximize recording of the oculomotor findings and their characterization [9]. Alexander’s law states that the amplitude of the spontaneous nystagmus increases when looking in the direction of the fast phase. Although this phenomenon is frequent in labyrinth or vestibular nerve lesions, it is also present, albeit less frequently with central lesions [10]. In addition, the nystagmus did not change in the different positions of gaze (unidirectional).
It is also expected that in cases of unilateral vestibulopathy, the remaining otolith function in the diseased ear and normal function from the other ear acts by modulating some of the characteristics of spontaneous nystagmus such as the velocity of the slow component or its amplitude; however this also occurs in cases of central vertical nystagmus [11]. Finally, the complete suppression of nystagmus when visual fixation was allowed is a typical finding for peripheral vestibular nystagmus as a result of normal cerebellar inhibition. All the nystagmus characteristics in this case pointed toward a peripheral lesion. Our point is to emphasize that horizontal nystagmus examination results alone must be interpreted with caution as central lesions can occasionally mimic labyrinthitis or vestibular neuritis. The analysis of a horizontal nystagmus is best performed in conjunction with the results of the head impulse test to distinguish central versus peripheral lesions.

4. The pattern of the VEMP abnormality was contrary to what we anticipated for a peripheral lesion involving the inferior vestibular nerve. The findings indicate a mildly abnormal response due to the increased latency of the first component (p13) but verify the integrity of the inferior vestibular nerve and its pathway to the upper cervical medulla. These results are incongruent however with the significantly decreased PSC gain, therefore, a lesion of the inferior vestibular nerve branch from the vHIT may be excluded [12]. The later component (n34p44), presumably of cochlear origin, was obtained and its amplitude appeared falsely higher than normal, due to decreased p13–n23 interpeak amplitude. To further complicate the pattern of findings, unexpected dysfunction was detected in the corresponding left VEMP side, suggesting multiple active and latent vestibular abnormalities. These findings have been previously reported in patients with MS [13].

5. Skew deviation. Peripheral vestibular lesions can rarely be associated with large amplitude skew deviation and the ocular tilt reaction, and this is an infrequent finding in acute peripheral vestibulopathies [14]. The cross-cover test usually detects vertical deviations greater than 3-prism diopters. The HINTS rule suggests that large amplitude skew deviation in the setting of an acute vestibular syndrome should alert clinicians to investigate the high probability of a central lesion, as observed in this case. This is particularly valuable in a patient with the nystagmus characteristics observed in this patient coupled with an abnormal head impulse test.

The neurological complementary examination provided the definite diagnosis of MS affecting mainly afferent and/or efferent fibers surrounding the right vestibular nucleus. A re-assessment of her past history uncovered an episode of postpartum urinary incontinence, in retrospect probably the initial manifestation of MS [15]. She also had a history of previous bilateral hearing loss in the course of what was diagnosed as acute unilateral otitis media; however, lack of conductive deafness or middle ear pressure changes in the left ear suggests that she had sensorineural hearing loss which spontaneously recovered. In view of recent findings, it is tempting to speculate that the episode of “acute otitis media” could represent a second relapse of demyelination. Hearing loss is an infrequent initial manifestation of MS, typically transient and unilateral in the acute state [16] but which eventually may lead to significant loss in the chronic stage.

In patients with vertigo, middle cerebellar peduncle lesions have been presented in cases of malformations [17], infarctions [18,19] and multiple sclerosis, as in our case [3]. The actual vestibular symptoms in our patient are due to a lesion in the proximity of the right vestibular nuclei (superior, medial and lateral) which explain nystagmus and head impulse response characteristics sparing the saccular projections that mainly go to the descending vestibular nucleus (normal right ear VEMP) and in the descending left medial vestibulospinal tract (abnormal left ear VEMP). The right facial numbness beginning simultaneously with the perception of disequilibrium would be due to the particular medial distribution of the lesion in the medulla.

In conclusion, this case represents the value of utilizing the HINTS rule [20]. The analysis of nystagmus direction and an abnormal head impulse test initially raised the question of an exception to the rule. However, the skew deviation detected by cross-cover testing motivated us to get additional history, neurologic testing and neuroimaging, concluding with a diagnosis of multiple sclerosis with the benefit of early intervention to procure a better neurological prognosis.

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