CASE REPORT

# Drop attacks and vertical vertigo after transtympanic gentamicin: diagnosis and management

## *Drop Attacks* e vertigine verticale dopo gentamicina transtimpanica: diagnosi e terapia

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Key words

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Parole chiave

*Malattia di Ménière • Terapia • Gentamicina transtimpanica • Drop attacks • Vertigine verticale*

Summary

Drop attacks represent a significant problem during the natural course of Meniere's disease. They are characterized by a sudden fall to the ground without loss of consciousness. Diagnosis is clinical and based on the typical description of the patient. Involvement of vertical canal is possible during Meniere's disease and also after gentamicin application. Treatment of drop attacks is still a matter of discussion; most cases have a benign course with spontaneous remission and no treatment is necessary. In severe cases, aggressive treatment (surgical or pharmacological) is necessary. A case of drop attack associated with vertical vertigo is presented. Vestibular tests were performed in order to assess the involvement of inner ear. Caloric test and ice water test reveal no response. Vestibular Evoked Myogenic Potentials are present even after high doses of gentamicin. Drop attacks and vertical vertigo can occur after transtympanic gentamicin and can be well managed with high doses of local gentamicin.

*Riassunto*

*I Drop attacks (DAs) rappresentano una condizione clinica molto fastidiosa che può presentarsi durante il corso della malattia di Ménière. Tipicamente il paziente riferisce di essere caduto improvvisamente senza perdita di conoscenza. La diagnosi è fondamentalmente clinica ed è basata sulla tipica descrizione del paziente. Il coinvolgimento dei canali semicircolari verticali è possibile sia durante la malattia di Ménière che dopo gentamicina transtimpanica. Ad oggi la terapia dei DAs non è stata ancora definita con precisione; la maggior parte dei casi presenta un decorso benigno con risoluzione spontanea, non necessitando quindi di alcuna terapia. In alcuni pazienti, data la gravità del disturbo, può essere indicato eseguire trattamenti più aggressivi, sia chirurgici che farmacologici. Viene riportato il caso di una paziente che ha iniziato a presentare DAs e crisi di vertigine su un piano verticale dopo applicazione di gentamicina transtimpanica. Una completa valutazione vestibolare è stata eseguita per cercare di valutare il reale coinvolgimento delle strutture dell'orecchio interno. La prova calorica e l'ice water test non dimostravano alcuna risposta. I VEMPs rimanevano evocabili anche dopo applicazione di alte dosi di gentamicina. In conclusione i DAs e le crisi di vertigine verticale possono presentarsi dopo terapia transtimpanica con gentamicina. Entrambe le condizioni possono essere gestite in modo adeguato con alte dosi di gentamicina applicata per via transtimpanica.*

## Introduction

Meniere's disease (MD) is a distressing disorder characterized by fluctuating hearing loss, tinnitus, episodic vertigo and aural fullness. From a physiopathological point of view, MD is a condition affecting the whole internal ear, even if the clinical presentation can depend on a parcellar involvement of the inner ear. The histopathological substrate of MD is endolymphatic hydrops (EH). Schuknecht and Igarashi observed that EH always involved the sacculus and the utriculus although hydrops in the endolymphatic compartments of the cochlea developed in completely different regions [1]. In other words, in MD, distension of the entire endolymphatic system can be found. At present, the mechanisms responsible for the fluctuating symptoms in MD remain to be fully elucidated; some of these probably result from

mechanical deformation of the membranous labyrinth [2]. EH can also alter the neural regulation of inner ear blood flow [2].
Most patients can only undergo medical treatment. In severe cases, when MD is disabling, ablative therapy can be used. Numerous reports have documented the efficacy of trans-tympanic gentamicin for the control of vertigo spells in patients with intractable MD [3 4].
Vertical crises, due to vertical canal involvement, are often underestimated because clinical symptoms due to lateral canal involvement are predominant. The incidence of drop attack (DA) is unknown, even if some Authors have estimated that the attacks occur in about 6% of MD patients [5]. Others have reported similar values [6] while others report very high values [7]. This difference is possibly due to different diagnostic criteria. Otolithic crises, also defined as Tumarkin crisis, are abrupt attacks of falling, without loss of consciousness. The attacks last a few seconds. According to Janzen and Russell, Tumarkin himself proposed that the cause was due to otolithic malfunction [8].
Spontaneous resolution of DAs is common but, in severe cases, aggressive treatment is necessary. DAs secondary to otologic causes must be recognized because, in severe cases, ablative surgery is curative [5].
To the best of our knowledge, this is the first report of a DA, associated with vertical vertigo, developed after trans-tympanic gentamicin.

## Case report

Personal experience in a 72-year-old white female suffering from definite right MD (class 4, PTA 80) is reported. After 6 months of medical treatment, with no benefit, it was decided to administer trans-tympanic gentamicin, using our standard preparation (see below). After 3 injections, performed at intervals of 20 days (an overall dose of approximately 35 mg of gentamicin), the patient started to suddenly fall down, without loss of consciousness; on one occasion, she fell to the ground hitting her face. She also reported vertigo spells, not associated with falling, lasting 1-2 hours, not associated with neuro-vegetative symptoms. Vertigo spells were typically associated with fullness and tinnitus. No deterioration in the auditory threshold has been reported in association with vertigo spells, possibly due to the severe reduction of pure tone average (PTA, 4 frequencies 0.5-1-2-3 KHz) in the right ear. When asked, the patient reported that the vertigo spells occurred in a sagittal plane and not in a horizontal plane; this condition was completely different from the situation before trans-tympanic treatment. The patient's quality of life was very poor and she was unable to look after herself. Caloric tests demonstrated areflexia of the right ear; an ice water test was not performed. The sacculo-collic reflex was intact. Due to the clinical condition, we decided to place a tympanostomy tube, in the right ear, and to start gentamicin application in order to obtain complete destruction of the inner ear. The patient was also informed about the possibility of surgical transmastoid labyrintectomy, as an alternative. The gentamicin solution was prepared using 2 ml of gentamicin sulphate (40 mg/ml) buffered with 1 ml of sodium bicarbonate; in this way, we obtain a final concentration of 26.7 mg/ml with pH 6.4. The patient was instructed to put about 1 ml of solution in the ear, 3 times a day. On days 1, 4, 7 etc., the patient returned to the hospital for bedside vestibular evaluation and audiometric test. We decided to stop the local applications after 35 days, when the patient reported that no more falls or vertigo attacks had occurred. The estimated total dose of gentamicin was about 900-1000 mg. After treatment, the patient complained of a marked disequilibrium and difficulty in walking. Caloric testing (Fitzgerald-Hallpike technique) and ice-water test demonstrated absence of lateral semicircular canal (LSC) function. VEMPs remained evokable. We, therefore, decided to start vestibular rehabilitation (VR). After 2 months, the patient was able to walk quickly and confidently; she had also returned to riding a bicycle. The Dynamic Gait Index (DGI) improved from 7, before VR, to 19, after VR. At the present time (10 months after the end of treatment), the patient is feeling well and DGI remains 7. Bedside vestibular examination revealed a right non-compensated vestibular paralysis. No further vertigo spells or drop attacks have been reported.

## Discussion

Drop attacks, first described by Tumarkin in 1936 as "otolithic catastrophe" [9], are characterized by a sudden falling to the ground without loss of consciousness. Usually, DA patients have no warning of an attack and know immediately where they are after hitting the ground. Diagnosis of DA is not always very easy; in typical cases, there is no doubt, in fact, patients usually describe a feeling of being "thrown to the ground" by a force. Since sensorium is preserved, syncope can be excluded. Albeit, in the presence of DA, cardiac and neurological causes must be ruled out. The fear of falling, caused by DAs, is an important cause of handicap in MD patients; in fact, patients with DAs are more dependent on visual and proprioceptive information [7]. Moreover, they tend to limit their activity and change their life-style.
DAs are thought to be caused by a sudden shift of otolithic maculae or by a rupture of the peri-lymph/endo-lymph balance. Another explanation is a possible mechanical deformation of the otolith organ which leads to activation of vestibulo-spinal reflexes [10]. DAs

are more frequent in the late period of MD [5], even if they can also occur in the earlier stages. Black postulated that erroneous information from otolithic maculae cause an incorrect alignment of the body axis relative to vertical gravity; thus the centre of gravity is moved outside the platform provided by the feet and consequently the patient falls to the ground [5].

As already mentioned, MD involves the whole inner ear; when the lateral canal is destroyed and the patient still complains of dizziness and vertigo, it is tempting to suspect that the latter are caused by the remaining function in vertical canals (VC) and otolithic organ [11]. Unfortunately, it is difficult to confirm this condition due to the lack of specific tests and to the difficulty in examining the patient during an attack. Undoubtedly, for DAs to develop, some vestibular function must be preserved [5].

In our patient, caloric function and ice water test demonstrated the absence of LSC function; the presence of VEMPs confirmed the integrity of the sacculo-collic pathway. This finding may explain the presence of DA. Due to the presence of a torsional nystagmus, observed during an attack, it is tempting to speculate vertical canal involvement. The nystagmus observation has been prolonged for at least 30 seconds and, throughout the observation, there was no change in direction or intensity. The nystagmus was observed only with the patient in a sitting position; no other positions were tested, due to the intense associated symptoms.

In our case, DAs are associated with vertigo spells of typical duration but of atypical direction. It is unclear why these attacks began after gentamicin application. We speculate that, in this patient, VC involvement was present before TG and that the VC symptoms were hidden by the presence of LSC involvement; furthermore, we cannot rule out the possibility that EH involved VC after trans-tympanic gentamicin. From these observations, we are strongly of the opinion that these manifestations are caused by the underlying pathology and its natural history.

Treatment of DAs is still controversial. Janzen et al. suggest conservative management in a DA patient, on account of the high rate of spontaneous resolution [8]. In their opinion, surgery is indicated when DAs become incapacitating, due to frequency, or severely affect the patient's life style [8]. Other authors suggest a first line treatment with drugs (diuretics, etc.); in disabling cases, surgery or gentamicin treatment are further options [12]. Vestibular ablation is highly efficacious for controlling disabling vertigo or falls secondary to MD [10]. Trans-tympanic gentamicin is an effective alternative in such cases [12]; indeed, good control of DAs has been reported in only about 60% of patients with DA [13]. Surgical treatment (labyrinthectomy or nerve section) can be effective also in older patients; it has been reported that the elderly show good compensation after ablative surgery [14]. Shunt procedures seem to be less effective in DA patients [5].

It should be borne in mind that, in older patients, comorbidity plays an important role in the compensation mechanism. The older the patient, the more important the continuation of exercises for months/years after treatment. Another golden rule is that in older patients with DAs, the search for a possible aetiology rather than MD, must to be performed very carefully.

In the case described here, the choice of gentamicin was taken with the patient. In our opinion, the presence of a remaining otolithic function is important for the patient to recover a better stability. What is really unclear is why VEMPs remain evocable after such dosage of gentamicin; it is tempting to hypothesise the presence of a mild fibrosis around the saccule or a genetic resistance to justify this finding. Albeit, we speculate that this function is not sufficient to re-start a DA.

## Conclusions

DAs can occur during the natural course of MD. Diagnosis of DA is based on the typical clinical presentation; other causes must to be ruled out especially in older patients. Conservative management can be proposed in mild cases; ablative treatment, either pharmacological or surgical, is effective in severe and disabling cases. The coexistence of vertigo spells can also be treated with these procedures.

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