AKINETIC SEIZURE WITHOUT LOSS OF CONSCIOUSNESS: MYASTHENIA SHOULD BE INCLUDED AMONG THE CAUSES. CASE REPORT

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ABSTRACT

Akinetic seizure means suddenly falling to the ground due to various causes that result in loss of balance, with or without alteration of consciousness, and usually followed by rapid recovery. There are two types: with or without loss of consciousness. In the first type syncope of various etiology is common, as are metabolic disorders such as hypoglycemia, hypoxia, toxicity (carbon monoxide), hyperventilation with hypocapnia, a few varieties of epileptic seizures, acute vertebral-basilar insufficiency. After describing the most common kinds of falls and their causes and effects, we will focus on those without loss of consciousness. The literature does not include diseases of the neuromuscular junction as a cause, but we describe a clinical case that suggests including myasthenia as a possible cause of falls without loss of consciousness.

***Key words**: falling, falls without loss of consciousness, myasthenia gravis, epilepsy, pseudo-seizures.*

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Introduction

Akinetic crisis means suddenly falling to the ground due to various causes that result in loss of balance, with or without alteration of consciousness, and usually followed by rapid recovery. They are observed primarily in the female gender. There are two types: with or without loss of consciousness.

In the first type syncope of various etiology is common, as are metabolic disorders such as hypoglycemia, hypoxia, toxicity (carbon monoxide), hyperventilation with hypocapnia, a few varieties of epileptic seizures, acute vertebral-basilar insufficiency. They may occur repeatedly over time and the patient may suffer injuries of varying severity, especially in the case of loss of consciousness, such as contusions, fractures, or skull trauma.

Akinetic crisis without loss of consciousness

This kind of fall is characterized by a sudden loss of strength in the lower limbs, and the ability to raise oneself after the fall. The etiology of this kind of crisis is difficult to identify. It is diagnosed differently and attributed to various mechanisms according to the patient's age, the specific motor and postural context, environmental conditions and the individual's clinical condition[1-3]. The causes of falls are common accidents in everyday life, such as ignoring steps, tripping over an obstacle, walking in the dark, losing one's balance, stepping backwards, going up or down stairs, slipping on wet ground or ice.

Other causes are certain pathological conditions such as hyperventilation, drop attacks, sudden changes in arterial pressure (usually hypotension), cardiac dysfunction (arrhythmia), cerebral dysfunctions following ischemic attacks in the carotid or vertebrobasilar area, ear canal alterations (vertigo,

Menière syndrome), progressive supranuclear palsy (PSP), Parkinson disease, cognitive deterioration, peripheral neuropathy, epilepsy, primary and secondary neuro-vegetative insufficiency, multiple system atrophy, iatrogenic syndromes (due to tricyclic antidepressants, antihistamines, levadopa, antihypertensives, beta-blockers, drug interactions), hypovolemia, hemorrhage, electrolyte imbalance, heat stroke, and psychogenic disorders[1-14]. The following are considered the most relevant neurological conditions responsible for akinetic seizures.

Drop attacks

These attacks are typical in senior patients, the causes of which are believed to be the hypersensitivity of the sinus carotid reflexes, a sudden drop in arterial pressure, or a myocardial dysfunction (arrhythmia) of varying duration with subsequent recovery[15-18]. They typically occur at night after being awakened by a need for micturition, in which the patients gets up quickly to go to the bathroom, falling while emptying his bladder (possibly facilitated by a Valsalva maneuver for prostate hypertrophy with the consequent obstacle of venous return). It is the most common event of multiple factors occurring at the same time, especially standing up quickly and the obstacle to venous return (Valsalva).

Cataplexy

These attacks occur in a sudden fall to the ground caused by a decrease in antigravity tone in the lower limbs, sometimes provoked by emotional events. The recovery follows after a few seconds or minutes without any alteration of consciousness. They sometimes occur in association with narcoleptic crises (drowsiness during the day) in the context of Gèlineau syndrome, sometimes symptomatic of an autoimmune process which damages the hypothalamic hypocretin secreting center, as may be seen in a reduced concentration in the patient's fluids (<110 ng/l).

Hyperekplexia

This is also a cause of sudden falls, an uncommon event that is not epileptic, provoked by a sudden jerk in subjects predisposed with autosomal dominant inheritance.

Progressive Sopranuclear Palsy

PSP is a fairly rare neurogenerative disease characteristic of adults and seniors. It is caused by widespread degeneration of cerebral neurons primarily in the mesencephalic region (a sign of flutter in encephalic RMN), with consequent compromising of ocular motility as well as balance, speech and swallowing. The initial symptoms are progressive limitation of the vertical motility of vision, especially looking down, axial muscular rigidity sudden falls (usually backwards), without loss of consciousness. It is more frequent after age 60, occurring in association with akinesia, hypertonia, hyper-extension of the body. The presence of sudden falls in these cases are not usually difficult to diagnose[19,20].

Multiple system atrophy

This form of atrophy includes multisystem clinical pictures, complex morphology, with a common presence of parkinsonism with muscular rigidity or hypertonia. Shy-Drager syndrome is a form of multisystem degeneration that includes autonomous nervous system dysfunction with cerebral ataxia, parkinsonism, partial spinal cord corticobulbar deficit, and electromyography alterations of the perineal plane. It is associated with Parkinsonism with severe orthostatic hypotension crises, sometimes extremely handicapping the patient due to the inability to stay erect. In contrast to Parkinson' disease, we find involvement of the cells of the intermediate lateral column of the medulla. The autonomous system insufficiency causes erectile dysfunction, urinary retention, fecal incontinence, hypohydrosis, reduced tearing and salivation in addition to orthostatic hypotension[21-23].

Epilepsy

In the context of epileptic seizures, petit mal or "absence" seizures include so-called akinetc/atonic ones, which are infrequent and characterized by sudden inhibition of postural tone, causing the child to fall to the ground without losing consciousness[5-9].

Psychogenic Seizures

There are heterogeneous manifestations, sometimes of the motor type, with possible falls to the ground often reported with "alterations of consciousness", in a specific emotional and behavioral context: blatant, histrionic, eccentric, emotionally immature, unstable mood, suggestibility, which may qualify for the category of somatic or conversion disorder (DSM-IV).

These events occur only in the presence of other people, and the symptoms are inconsistent with organic disease: when the patient is feeling bad (mood of varying duration), inconstant (alternating

with periods of feeling well), often associated with manifestations of a different category such as the classic opisthotonus crisis, unusual and variable gesticulations (very different from the stereotyped manifestations of epileptic seizures, sometimes accompanied by shouting, crying, apparent self-injury; they are repeatable and inducible, there are no EEG alterations in the periods between seizures nor confusion after the seizure[5-9,24]. A functional akinetic seizure may be easily suspected when the patient history includes:

• sensory or motor manifestations that develop in a sequence that is polymorphic and anarchical, with casual involvement of the limbs

• oscillating movement of the pelvis or head, opisthotonus posture, accompanied by shouting, crying or laughter

• absence of the post-seizure phase relaxation of the sphincters, trauma from falling to the ground, nor biting of the tongue

• common in the female gender, with unpredictable progression

• never occurring at night or when the patient is alone

However, it should be kept in mind

• bizarre automatism complex can occur with frontal lobe seizures

• frontal lobe seizures may have bilateral convulsive movements without impairment of consciousness

• post-ictal confusion is often absent after frontal lobe seizures

• aggressive and emotional behavior can occur after epileptic seizures (American Epilepsy Society 2010)

• in some cases certain psychogenic seizures alternate with true epileptic seizures in the same patient[5-7].

Such patients may monopolize the family and physician's time, and neuroradiological/neurophysiological testing and treatment are fruitless.

Case Report

The case described here suggests another possible clinical condition responsible for sudden and unpredictable falls without loss of consciousness. An adolescent female aged 11y, 11m in good general health suddenly experienced falls to the ground without losing consciousness and with spontaneous recovery (standing up). There was no forewarning of the fall, and a tendency for the event to be repeated with variable frequency (2-6/week) and no precipitating cause. She was admitted to the pediatric ward where acute and chronic abnormalities were excluded (cardiological, metabolic, encephalitic, epileptic), and a neurophysiological evaluation was requested.

The patient was accompanied by both parents who were naturally worried, with the mother apparently very protective and at the same time intolerant toward her daughter due to the presumed capriciousness and voluntary nature of the symptoms, especially after the doctors failed to find any organic cause of the condition. The patient seemed tired of the many tests and annoyed by the mother's impatience (who constantly held her daughter's hand), but without wanting the mother to leave. The family context and personal background seemed anxiety-ridden. The neurologic examination was also negative, which was compatible with a diagnosis of functional akinetic seizure.

The usual neurophysiologic evaluations (electroneurography, electromyography) failed to reveal any abnormality. The clinical examination was broadened with an evaluation of the capacity to maintain an extreme positions of gaze. The girl withdrew her gaze quickly, and stopped looking at the object placed in front of her eyes in various sectors of her visual field, without saying why, seemingly consistent with capriciousness.

We then attempted to perform repetitive nerve stimulation, with the expectation that the patient would refuse. But she cooperated willingly, which allowed us to perform a complete battery without artifacts, although only at low stimulation frequencies (3 and 5Hz), to avoid the patient withdrawing from the examination. The results are reported in table 1.

As can be seen from the results, repeated stimulation of the ulnar nerve, deriving from the abductor of the fifth finger, the accessory spinal nerve deriving from the superior trapezius muscle, the facial nerve deriving from nasal to the orbicolaris of the eye muscles, the fibular nerve deriving from the ext. dig. brevis, the medial nerve deriving from the abd. poll. brevis, right, with stimulation from 3 to 5 Hz, showed homogeneous pathological variations of the amplitude/area from the fifth CMAP compared to the first CMAP, in all the muscles examined. The patient then underwent a test for anti-AChR antibodies, which found an elevated level. Treatment with low dose cholinesterase inhibitor led to a satisfying and stable regression of the current symptoms five months from the beginning of therapy[25-28].

Patient name:		V.A.	**Patient ID:**	129-14	**Age:**	11 Anni 11 Mesi				
Sex:	Female	**Department:**	Pediatrics							
Stim. Rep.										
Muscolo / Train	**Ampl. mV**	**Amp. D. 1 %**	**d. Ampl2 %**	**Fac Ampl %**	**Area mVms**	**d. Area1 %**	**d. Area2 %**	**Fac Area %**	**Rate pps**	**Time**
D ABD POLL BREVIS - Default										
Baseline	7.7	-6.7	-5.4	100	27.9	-14.9	-7.4	100	3	0:00:00
Facilitation	9.3	-13.5	-8.9	121	33.8	-15.7	-11.5	121	3	0:01:01
@0:30	9.3	-15.4	-8.9	120	34.3	-17.4	-13.3	123	5	0:02:03
@1:00	9.6	-16.9	-12.7	124	34.5	-19.5	-15.3	124	5	0:02:58
D TRAPEZIUS (U)										
Baseline	5.9	-17.6	-15.6	100	42.6	-24.7	-22.4	100	3	0:00:00
Facilitation	5.7	-17.9	-16.9	97.8	43.6	-25.9	-24.9	102	3	0:01:17
@0:30	5.7	-21.3	-16.3	97	43.9	-32.9	-28.7	103	5	0:02:52
@1:00	5.6	-22.5	-19.5	96.5	42.7	-31.3	-27.8	100	5	0:04:00
D ORB OCULAR - Default										
Baseline	1.4	-30.1	-31.7	100	4.3	-37.4	-44.8	100	3	0:00:00
Facilitation	1.5	-32.6	-30.7	106	4.3	-39.2	-36.3	99.8	3	0:01:07
@0:30	1.6	-41.5	-32.3	112	4.4	-52.7	-36.5	101	5	0:02:21
D NASALIS										
Baseline	2.1	-14	-28.2	100	4.7	-16.5	-34	100	3	0:00:00
Facilitation	2.1	-14.7	-17.4	100	4.7	-15.8	-20.9	99.3	3	0:01:11
D ABD DIG MIN (UL)										
Baseline	5.4	-18.2	-12	100	16.9	-19.8	-11.9	100	3	0:00:00
Facilitation	5.3	-19.1	-10.5	98.4	16.4	-22.9	-14	97	3	0:01:01
@0:30	5.5	-25.8	-11.6	102	17.1	-29.4	-18.8	101	5	0:02:55
@1:00	5.5	-23.1	-10.8	102	16.6	-27.2	-15.6	98.5	5	0:03:57
D EXT DIG BREVIS - Default										
Baseline	8.8	-13.7	-8.1	100	25.2	-16.6	-13	100	3	0:00:00
Facilitation	9	-14.4	-9.3	102	25.4	-17.2	-12.8	101	3	0:01:06
@0:30	8.7	-11.4	-4.3	99.5	25.7	-18.8	-12.8	102	5	0:02:08
@1:00	8.8	-13.2	-6.4	100	25.6	-17.7	-12.1	101	5	0:03:06

Table 1: Multiple repetitive nerve stimulations.

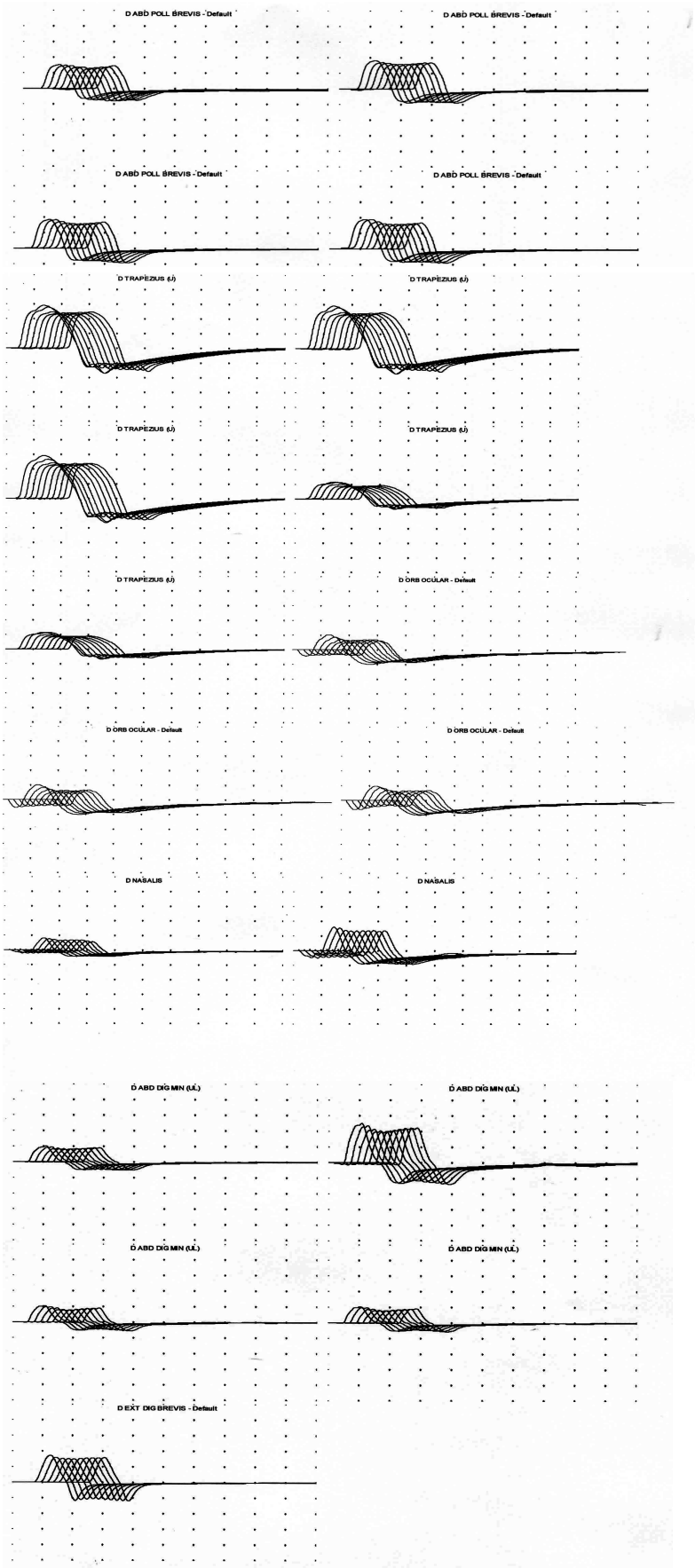

Fig. 1: Multiple repetitive nerve stimulations.

Conclusions

The clinical case described justifies the following considerations.

1. Confirmation that the pathology of neuromuscular junction should be included among the possible causes of akinetic seizures without loss of consciousness.

2. Psychiatric diagnosis should always follow rather than precede neurological testing to exclude all organic causes.

3. In cases with an unclear clinical picture, it is advisable to consider inusual diagnostic possibilities.

References

1) Meissner I, Wiebers DO, Swanson JW, O'Fallon WM., *The natural history of drop attacks*. Neurology., 1986,vol. 36, *1029-34*.
2) David J. Thurman, MPH, Judy A. Stevens, and Jaya K. Rao, MD, *MHS Practice Parameter: Assessing patients in a neurology practice for risk of falls (an evidence-based review) Report of the Quality Standards Subcommittee of the American Academy of Neurology*, Neurology February 5, 2008 vol. 70, 6, *473-479*.
3) Stevens D L and Matthews W B, *Cryptogenic Drop Attacks: An Affliction of Women in Br* Med J., 1973, pp. *439-442*.
4) Nevitt M C, Cummings S R, Kidd S, Black D *Risk Factors for Recurrent Nonsyncopal Falls. A Prospective Study* JAMA. 1989; 261(18): *2663-2668*.
5) Richard R. *Differential diagnosis of sleep disorders, non epileptic attacks and epileptic seizures Current Opinion in Neurology*: April 1998 - Vol. 11 - Issue 2, *135-139*.
6) Thijs R D, Bloem B R, van Dijk J G. *Falls, faints, fits and funny turns Journal of Neurology* , February 2009, Vol. 256, Issue 2, *155-167*.
7) Devinsky O, Sanchez-Villasenor F, Vazquez B, Kothari M, MD, Alper K, and Luciano D *Clinical profile of patients with epileptic and nonepileptic seizures* Neurology 1996;46: *1530-1533*.
8) Martin R, Burneo JG, Prasad A, Powell T, Faught E, Knowlton R, Mendez M, Kuzniecky R *Frequency of epilepsy in patients with psychogenic seizures monitored by video-EEG Neurology*. 2003 Dec 23; 61(12): *1791-2*.
9) Williams DT, Ford B, Fahn S. *Treatment issues in psychogenic-neuropsychiatric movement disorders,* 2005. Adv Neurol.; 96: *350-63*. Review.
10) Rampello L, Raffaele R, Vecchio I, Pistone G, Brunetto M.B, Malaguarnera M. *Behavioral changes and hypotensive effects of thioridazine in two elderly patients with traumatic brain injury* (2000). Gazzetta medica italiana. Archivio per le scienze mediche, vol. 159, *1-3*.
11) Rampello L, Battaglia G, Raffaele R, Vecchio I, Alvano A. *Is it safe to use antidepressants after a stroke?* (2005). Expert opinion on drug safety, vol. 4(5), *885-897*.
12) Rampello L, Vecchio I, Malaguarnera M, Malaguarnera G, Rampello. *Diabetic neuropathy. Clinical varieties L* (2012). Acta Medica Mediterranea, vol. 28, *127-132*.
13) Rampello L, Vecchio I, Malaguarnera M, Rampello L. *Axonal and demyelinating motor neuropathies. Differential diagnosis* (2012). Acta Medica Mediterranea, vol. 28, *139-140*.
14) Rampello L, Vecchio I, Battaglia G, Malaguarnera G, Rampello L *Diabetic neuropathy. Elements of epidemiology and pathophysiology* (2012). Acta Medica Mediterranea, vol. 28, *219-223*.
15) Ricceri R ,Leanza, R , Lentini, F, Rampello, L, Chisari, CG, Rampello, L Evolution of the concept of vascular dementia Acta Medica Mediterranea, 2013, Volume:29, Issue: 1, *99-101*.
16) Ricceri R, Lentini F, Leanza R, Rampello L, Rampello L. *Know to prevent: risk factors of the vascular dementia* (2013). Acta Medica Mediterranea, vol. 29, *109-113*.
17) Rampello L, Alvano A, Battaglia G, Raffaele R, Vecchio I, Malaguarnera M. *Different clinical and evolutional patterns in late idiopathic and vascular parkinsonism* (2005). Journal of Neurology, vol. 252(9), *1045-1049*.
18) Zelante G, Catalano A, Ricceri R, Rampello L, Rampello L. *Subcortical vascular dementia: lights and shadows* (2012). Acta Medica Mediterranea, vol. 28, *45-52*.
19) Rampello L, Ruggieri M, Vecchio I, Battaglia G, Chisari C.G, Malaguarnera M, Zelante G, Catalano A. *Amyotrophic lateral sclerosis: differential diagnosis with cervical myeloradiculopathy* (2011). Acta Medica Mediterranea, vol. 27, *149-152*.
20) Rampello L, Butta V, Raffaele R, Vecchio I, Battaglia G, Cormaci G, Alvano A *Progressive supranuclear palsy: a systematic review* (2005). Neurobiology of disease, vol. 20(2), *179-186*.
21) Rampello L, Vecchio I, Malaguarnera M, Malaguarnera G, Rampello L. *Parkinson's disease: knowing it to recognize it* (2012). Acta Medica Mediterranea, vol. 28, *113-116*.
22) Rampello L, Cerasa S, Alvano A, Butta V, Raffaele R, Vecchio I, Cavallaro T, Cimino E, Incognito T, Nicoletti F. *Dementia with Lewy bodies: a review* (2004). Archives Of Gerontology And Geriatrics, vol. 39(1), *1-14*.
23) Rampello L, Chiechio S, Raffaele R, Vecchio I, Nicoletti F. *The SSRI, citalopram, improves bradykinesia in patients with Parkinson's disease treated with L-dopa* (2002). Clinical Neuropharmacology, vol. 25(1), *21-24*.
24) Rampello L, Battaglia G, Rampello L, Malaguarnera M. Bilateral benign blepharoclonus (2009). Clinical Neurology And Neurosurgery, vol. 111 (5), *480-481*.
25) Meriggioli MN1, Sanders DB *Autoimmune myasthenia gravis: emerging clinical and biological heterogeneity* Lancet Neurol. 2009 May; 8(5): *475-90*.
26) Rampello L, Ruggieri M, Vecchio I, Battaglia G, Chisari C.G, Malaguarnera M, Zelante G, Catalano A. *Asthenia: a mask for many identities. The role of dysfunction of the neuromuscular junction* (2011). Acta

Medica Mediterranea, vol. 27, *149-152*.
27) Migliore M, Alongi G, Rampello L, Astuto M. *Video assisted trans-cervical thymectomy. A minimally invasive approach to treat non-thymomatous myasthenia gravis*. (2013) Annali Italiani Di Chirurgia, vol. 84, *667-670*.
28) Migliore M, Vecchio I, Rampello L, Borrata F, Astuto M, Rampello L. *Multisciplinary approach of non-thymomatous myasthenia gravis*. (2012) Acta Medica Mediterranea, vol. 28, *211-213*.

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