MULTIDISCIPLINARY APPROACH FOR THE DIAGNOSIS OF NEUROGENIC VASOVAGAL SYNCOPE

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ABSTRACT

Syncope is a common clinical problem, with a relatively simple etiology but with a complex pathogenesis. There are many clinical varieties, thus requiring multiple clinical, instrumental, and multi-disciplinary investigations. The most common variety is so-called vasovagal syncope, frequently observed at a neurological level. Often, however, syncope requires an accurate differential diagnosis with two other diseases with which it shares similarities and differences, such as epileptic seizures and psychogenic crisis.

Key words: Vasovagal syncope, syncope, epilepsy, psychogenic crisis, differential diagnosis, pain.

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Disorders of consciousness, either real or fictitious, are among the most important occurrences in neurological practice. In this context, the possible etiologies are unfortunately numerous and thus constitute a severe challenge for the neurologist involved.

Syncope is a relatively frequent occurrence. It consists in a sudden and transient loss of consciousness and postural tone of a person of any age, most often in the feet, resulting in a fall and recovery a few minutes later, in the absence of neurological sequelae.

The cause of syncope consists of a transient critical reduction of cerebral blood flow well below the 52 ml of blood per 100 g of brain tissue per minute, a value considered optimal for a good oxygenation and nutrition of the central nervous tissue.

The pathogenic mechanisms of syncope are numerous and very complex ranging from the fall of the sympathetic tone to the postoperative tone: in this brief review we will simply mention them, paying more attention to the differential diagnosis with similar but different symptoms[1-2].

In a nutshell, the pathogenesis comprises three main mechanisms:

1. Vasodepressor effect (fall in sympathetic tone) and/or vasovagal effect (parasympathetic hypertonia with bradycardia): neurogenic syncopes

2. Deficit of venous return due to lack of sympathetic innervation of blood vessels and compensatory autonomic mechanisms

3. Decreased cardiac output due to alterations of the myocardium, valves, chambers or heart rhythm, to blood clots, aortic stenosis or hypovolemia (hemorrhage, dehydration).

Several conditions may contribute in varying degrees to support one of the aforementioned pathogeneses: malfomative, metabolic, vascular, dysfunctional, infectious, dysimmune, traumatic, etc. Therefore, the subject who has experienced a syncopal episode deserves a careful multidisciplinary assessment aimed at identifying the underlying etiology to the point that specific dedicated centers have been established to minimize the risk of mis-

diagnosis and disregard of potentially life-threatening occurrences, with the assistance of cardiologists, neurologists, neurophysiologists, pulmonologists, internists, and sometimes even with cardiothoracic surgeons with specific training for this role (multidisciplinary group).

The syncopal varieties directly concerning the neurologist are those known as neurogenic. The varieties of neurogenic syncopes most commonly observed in current practice are the so-called vasovagal syncopes[3].

They are the common episodes of "fainting", sometimes with familial imprint, that variously affect the general population, caused by strong emotions, intense pain[4], unusual aerobic or anaerobic muscle strain, sight of blood, traumas, defecation, urination, coughing, swallowing cold drinks, Valsalva maneuver or combination thereof.

Pathogenetic factors are included in the first case listed above: fall in sympathetic tone (hypotension) and/or increased vagal tone (bradycardia) with a consequent drop in blood pressure and poor cerebral blood flow. Loss of consciousness, when it occurs, is typically preceded by a feeling of malaise defined lipothymia, lasting about 5-6 seconds, consisting of vertigo, faintness, weakness, sweating, pallor, tinnitus, blurred vision, nausea and sometimes vomiting, variously associated with each other, if subjects are able to lay down in a supine position, they can also avoid the onset of syncope and hence the loss of consciousness; otherwise the latter is the inevitable result of the malaise, with a fall to the ground that may be traumatic at times. EEG recordings at this stage make it possible to detect a widespread slowdown in brain electrical activity (theta or delta rhythm), which is an index of the underlying brain condition.

In most cases, the new posture allows the recovery of a good cerebral blood flow resulting in recovery of consciousness. In the event that instead, the supine position does not allow for this effect (for example, due to cardiac arrest) because the acute cerebrovascular failure lasts more than 13-15 sec., syncope develops into convulsive syncope: the patient lying on the ground, motionless, hypotonic, pale, and unconscious, suddenly starts to convulse as in the case of a generalized tonic-clonic seizure, with possible sphincter incontinence and tongue biting (rare in simple syncope). EEG recordings at this stage detect a flattening of brain electrical activity: these are the forms that, if not directly observed by a careful eye, as is most often the case, pose serious problems of differential diagnosis with epileptic seizures. If the question is not clarified, the problems for the patient increase, as anticonvulsant therapies do not help cardiac patients at all and sympathomimetic drugs are of no help to epileptics.

The evaluation of an individual who has suffered syncope requires a careful case history, by performing a thorough neurological physical examination in search of even mild sensorimotor, relational, practognosic, and cognitive deficits, Doppler ultrasound of the SAT, neuroradiological examination of the brain, and an accurate clinical and instrumental cardiological evaluation (ECG, Holter-ECG and Holter, echocardiography).

Simple, uncomplicated vasovagal syncope, without documented cardiac, dysautonomic, metabolic, brain and other structural or dysfunctional alternations, is not an alarming occurrence, but quite common, not to be exaggerated and, if possible, to be prevented with targeted measures and precautions suggested by the attending physician: avoid abrupt changes from reclined to erect position, prolonged stays in overly heated rooms, protracted fasting, overexertion without prior training, etc.

The most frequent differential diagnosis is the one between syncope and an epileptic seizure or a pseudo-epileptic seizure[5-6].

Epileptic seizures, of course, with clinical signs similar to syncope, are possible but not common. The difficulty arises from the fact that neurologists seldom witness the event, whereby the distinction is made based on the deficient clinical history provided by family members, often distracted by the alarmed participation in the event so that critical elements and details essential for diagnosis remain vague.

One solution, often suggested at a neurological level, proves to be reliable and it consists in recording the event on film. This is now possible thanks to the widespread availability of video cameras and mobile phones equipped with video recording function[7-8].

The proposed guidelines for the differential diagnosis of the 3 clinical conditions should include the distinction between their progression, the type of onset, the presence of premonitory symptoms, phenotypic manifestation, facial color, critical muscle tone, critic and intercritical EEG, time of onset, critical traumas, possible sphincter incontinence, memory of the event, recovery of consciousness, frequency of attacks, any hematological alterations during the crisis (if any), social context, and posture:

• Syncopal crises have a one-time occurrence, while seizures tend to have a chronic course with variable frequency, ranging from frequent daily events to annual occurrences, and are quite sensitive to treatment in 75% of cases; the pseudo-seizures have an unpredictable course, with long periods of remission that alternate with periods of frequent manifestations that are difficult to therapeutic approach;

• The onset of the epileptic event is certainly the most acute, almost "ictal", similar to what is observed in some painful attacks[9], while that of syncope, though rapid, progresses in a few seconds, coinciding with the duration of the lipothymic stage; the pseudo-seizure has no rules, but it never appears so acutely;

• Syncope usually has prodromal symptoms that are those of said lipothymic stage. The epileptic seizure may have an aura, usually of the same type, connected with the function of epileptogenic focus, well known to patients who can use it to protect themselves from the effects of the epileptic seizure; the pseudo-seizures may be preceded, albeit at an extremely variable distance from the critical event, by intense or significant emotional stress;

• The typical manifestation of syncope is with the characteristic akinetic crisis with fall to the ground in a state of total muscular hypotonia; epileptic crisis generally have, depending on the variety, hypotonic and/or hypertonic stages; the pseudo-seizures is extremely variable in terms of phenomenal expression without a stereotypical course as the former;

• Typically, during syncope, the color of the subject's face is pale and cadaverous; epileptic patients are usually cyanotic, while in pseudo-seizures there are no changes in facial complexion, save for occasional redness with sweating in varieties with pseudo-convulsive manifestations: in these cases, please bear in mind the pathognomonic resistance to the passive opening of the eyelids;

• The critical EEG is slowed in syncope (theta-delta rhythm), with the typical critical changes in epilepsy (spikes, poli-spikes and spikes-and-wave), while it is normal in pseudo-seizure;

• The intercritical EEG is always normal in syncope and it may be so also in epileptics in the absence of the stigmata highlighted especially with activation techniques (hyperpnea, SLI, sleep deprivation). It is absolutely normal in pseudo-seizure;

• Typically patients who manifest a syncope are standing, rarely sitting, never lying in a supine position; epileptic patients have no preferences of posture at the onset of the seizure, while the pseudo-crisis has no preferences of posture at onset;

• Both epileptics and patients with syncope can suffer injuries during the crisis, but the risk is definitely greater for the former, while in pseudo-seizure the risk is zero;

• Critical sphincter incontinence is almost an exclusive of epileptic patients, exceptionally of syncope, and never of pseudo-seizure;

• The memory of the critical event is always absent in epilepsy and syncope, while it is only unacknowledged or concealed in pseudo-seizure;

• Recovery of consciousness is instantaneous in syncope, very slow in epilepsy, with frequent confusional sequelae, while in pseudo-seizure consciousness is never lost;

• The frequency of the crisis is rare and occasional in syncope, very variable in epilepsy (from many a day to few or less a year), unpredictable in pseudo-seizure, which has long periods of remission and clusters of relapse, scarcely sensitive to the various treatments;

• Although it is not frequently used and its reliability has not been attested yet, only in epilepsy is there a possible critical increase in prolactin or CK, not in the other two diseases;

• It is significant to consider that the syncopal crisis and pseudo-seizure never occur during sleep, while in the case of epilepsy this eventuality is possible and at times preferential;

• It should finally be mentioned that syncope and epileptic seizures do not have a prevalence of existential context, while pseudo-seizure certainly does, giving priority to family reunions, large parties, weddings and all occasions of family meetings.

Then there is the possible coexistence, in the same patient, of epileptic seizures and pseudo-seizures. None of the parameters above allows us to make a certain differential diagnosis, but their simultaneous assessment, an accurate clinical history, research and the identification of possible secondary gains, the perception that a patient has a passive or active role in the illness, the quality of the emotional resonance of critical attacks, and the presence or absence of bystanders during the seizures are excellent guiding elements for diagnostic purposes.

	Syncope	Epilepsy	Pseudo-seizure
Circadian recurrence	never during sleep	also during sleep	never
Social context	indifferent	indifferent	gatherings
Posture	erect	always	indifferent
Frequency	occasional	chronic	unforeseeable
Eliciting factors	frequent	absent	non apparent
Prodromes	lipothymic	rare (aura)	absent
Onset	progressive	ictal	variable
Face eyelids	pale	cyanotic	resist. opening eyelids
Muscle tone	hypotonia	hypo/hypertonia	variable
Phenotype	akinesia	hypo/hyperkinesia	hypo/hiperkinesia
Traumas	rare	possible	absent
Tongue biting	rare	possible	absent
Urinary incontinence	rare	possible	absent
Duration	seconds	sec/min	sec/hours
Post-seizure confusion	absent	constant	absent
Critical EEG	θ/δ rhythm	typical	normal
Intercritical EEG	normal	variable	normal

Table 1: List of the main similarities and differences between syncope, epilepsy and pseudo-seizure (so-called functional or psychogenic seizures).

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