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SYNCOPE OR EPILEPTIC FITS?

Some examples of diagnostic confounding factors

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ABSTRACT - Syncope is a condition often misdiagnosed as epileptic seizures. However, the differential diagnosis between both conditions can be quite difficult, even for well-trained physicians. Four cases of epilepsy and/or syncope are reported, to exemplify this situation. Each case is discussed individually, and the confounding factors are analyzed.

KEY WORDS: epilepsy, syncope, seizures, differential diagnosis, non-epileptic events.

Síncopes ou crises epilépticas? Alguns exemplos de fatores de confusão diagnóstica

RESUMO - Síncope é uma condição freqüentemente diagnosticada equivocadamente como crise epiléptica. No entanto, existem algumas situações nas quais a diferenciação entre ambas pode ser difícil até mesmo para alguns médicos ou especialistas bastante familiarizados com essas condições. Quatro casos de pacientes com epilepsia e/ou síncope procuraram os autores para elucidação diagnóstica. Cada caso é discutido individualmente, assim como os potenciais fatores de confusão são analisados.

PALAVRAS-CHAVE: epilepsia, síncope, crises, diagnóstico diferencial, eventos não-epilépticos.

An old say states that 80% of general diagnosis are attained through clinical history, further 10% through physical examination; and another five percent through ancillary investigation. The last five percent of cases are not determined at all. Diagnosing epilepsies is not an exception to this concept and if there is a rule at all, that is that "when first seeing a patient we must rely more on a careful history taking and physical examination than on a high-tech diagnostic work-up". A classical example for this view is the differential diagnosis between epilepsy and syncope. Although most patients with these conditions show clear-cut differences on their clinical presentation, for some atypical cases even an experienced neurologist may have difficulties in reaching a precise diagnosis.

The scope of this paper is not aimed to cover all the aspects involved in epileptic or syncopal disorders, but to describe and discuss some atypical cases in which the diagnosis was a quiz. Puzzling cases should not be taken as a rule, but knowing them may keep the readers aware of the some pitfalls that should be kept in mind.

CASES

Case 1 – A six-year-old girl presented several spells along the preceding two years. Two previous EEG had shown bilateral central-temporal spikes whose frequency and amplitude increased with sleep. Cranial MRI suggested a questionable atrophic lesion in the left central area. She had thalassemia and was taking oxcarbazepine 300 mg twice a day based on a previous presumptive diagnosis of benign rolandic epilepsy. Her parents reported oxcarbazepine-induced weight-gain. However, her clinical history was suggestive of syncopes, instead of seizures. She had had pancreatic insufficiency in infancy and was allergic to insect bites. Her mother had thyroid disease and low blood pressure. Her father had a past history of syncopes. Her two elder brothers were healthy. There was no family history for epilepsy. Inten-

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ding to exclude reflex epilepsy with giant evoked responses, a new EEG with percussion of her toes was performed, and only confirmed the previous pattern seen in rolandic benign epilepsy. A tilt-test was positive for vasovagal syncope. Since the patient had never presented rolandic seizures, oxcarbazepine was withdrawn and fludrocortisone 0.1 mg/day was started with complete resolution of syncopal events. After two years of therapy, fludrocortisone was successfully withdrawn and she remained asymptomatic.

Comments: Although this patient's interictal EEG was suggestive of benign rolandic epilepsy[1], her spells did not. Benign rolandic epilepsy seizures typically begin with sensory-motor symptoms, usually with a smell-oral or a lower limb distribution, either case showing Bravais-Jacksonian progression and associated with phonatory blockage[1]. Abnormalities similar to those presented by patients with benign rolandic epilepsy can be seen in 30% of their relatives, but also in 5% of pediatric patients randomly selected[2]. As an isolated finding, epileptiformactivity was found in the EEG tracing of 0.5% of 13,658 young adult volunteers[3]. This case illustrates that even a clear-cut abnormal EEG shall never be considered evidence of disease (epilepsy) per se, and that the physician must rely more on the clinical history data rather than in ancillary data. Finally, even in children, the tilt-test can be useful in the diagnosis of syncope[4].

Case 2 – A 16-year-old white male attended due to two spells. The first one had occurred six months before, after rising from a coach. He became pale and fell on the floor, without involuntary movements, and was regaining clear consciousness soon afterwards. Five days before his appointment, he presented one more spell also after rising up from bed and walking a few steps: he yelled a cry and fell in "convulsion" (sic). He regained consciousness but was confused for half an hour. He had allergic rhinitis. He had a past history of repaired inguinal hernia at 40 days of life, hydrocele surgery, when three-years-old, appendectomy, and a tonsillectomy. His mother had migraine. Physical general examination was unremarkable. Carbamazepine 200 mg twice a day was started. His EEG and CT-scan were normal. A few months before, he started to present migraine. A tilt-test disclosed postural tachycardiac syncope associated with vasovagal manifestations. He was instructed to be kept well hydrated and to avoid standing up abruptly. After four years of follow-up he had presented no further seizures nor syncope episodes, but only mild episodes of faintness.

Comments: The normal routine EEG presented by this patient should not be used to rule out epilepsy, since at least 6 exams are necessary for achieving an 77% sensibility yield[5]. Not only syncopal attacks may be taken as epileptic seizures[6,7], but also "syncopal" spells might prove to be epileptic[8]. Thus, characterizing each episode of loss of consciousness through history may be important, for this since this patient presented both an epileptic seizure (one episode) and a syncopal episode. This approach might prevent an equivocal impression of unsuccessful therapy for epilepsy, as it may occur for a given epileptic patient with associated syncopes. However, even in proven epileptic patients, a careful cardiovascular evaluation should be pursued, since epileptic seizures may trigger syncopal episodes by inducing to bradycardia and sinus arrest, and some anti-epileptic drugs may predispose to syncope episodes[9].

Case 3 – A 25-year-old woman was attended because of three spells in two days in a month. In the last one, before her appointment, she was taken to an emergency room where she received a loading intravenous dose of phenytoin. Nine years before she had had a resected right hippocampal astrocytoma. At that time she presented refractory epileptic seizures and in the last four years her antiepileptic medication could be stopped. After surgery she did not report any further epileptic fit. The anamnesis revealed that some of the last spells had occurred during venipuncture and "spontaneously" when the patient was in closed environments, such as crowded buses or churches. This description was more in keeping with syncopes than with epileptic seizures, either partial or generalized. Her EEG disclosed left temporal slowing. Cranial MRI revealed right temporal gliosis. A tilt test triggered a vasovagal syncope. The patient is on atenolol 25 mg qd at morning without recurrence of the spells.

Comments: This case illustrates that a past history of epilepsy, and even severe refractory temporal lobe seizures should not always lead to the diagnosis of relapsing epileptic seizures. Temporal lobe epilepsy has the best response to epilepsy surgery, resulting in complete control of seizures in about 87.7% of the cases with mesial atrophy[10], an index that may be even better - 80% to 100% - in case of combined complete lesionectomy associated to anterior temporal lobectomy for the removal of a temporal lobe[11,12]. Even patients with proven epileptic seizures can present other types of spells such as non-epileptic psychogenic phenomena[13]. In this patient, the correct diagnosis was suggested by the previous history of venipuncture fits, more likely to be reported in children[14], and through a clear history of long remission of the epilepsy after the surgical approach.

Case 4 – A 22-year-old young white woman came to us for a second opinion about the treatment needing for her epilepsy. Her spells had started at the age of nineteen years. She described a sensation of hotness and a *"blank"*. Episodes had occurred while taking the bus or inside the bathroom. At one of the episodes, while in a bus, she presented a versive movement of her head to the right and some clonic jerks of her limbs. She

Table 1. Clinical differences between syncope and epileptic seizures.

	Syncopes	Epileptic seizures
Triggers	frequent	rare
Preceding symptoms	nausea, visual blurring, epigastric sensation, heat, headache, tinnitus	sensorial, psychic, somato- sensory "auras" or motor phenomena
Blanks	"fading away"	"disconnection" or abrupt loss
Fall	slow, flacid	fast, tonic
Ictus	flacid, tonic anoxic seizure	tonic-clonic, tonic
Duration	~ 15 s (3 s - 30 s)[9]	GTCS 30 s - 5 m[30] SGTCS ~ 62 s (16 s - 108 s)[31]
Post-ictal	somnolence, headache	confusion, somnolence, headache

~, mean; s, seconds; m, minutes; GTCS, generalized tonic-clonic seizure; SGTCS, secondarily generalized tonic-clonic seizure.

brought a high-quality EEG tracing revealing slow waves with sharp morphology at hyperventilation, and a head MRI showing asymmetric lateral ventricles, i.e. the left lateral ventricle considered larger. Her physical and neurological examinations were unremarkable. A tilt-test disclosed vasovagal syncope, with symptoms very alike to those previously and spontaneously presented. She was on atenolol 25 mg qd without further spells.

Comments: This case illustrates how unremarkable findings in ancillary investigation can mislead to the diagnosis of epilepsy. The slowing of the EEG background at hyperventilation may be present with sharp morphology, as many other harmless epileptiform patterns, such as psychomotor variant, phantom spike-and-waves, wicket spikes, vertex waves of sleep, positive occipital transients of sleep and others[15]. Although well described in the available literature, these epileptiform patterns may sometimes be confused as irritative activity by a less attentive EEG reader, and lead to unnecessary therapy. CT-scan brain images may also show asymmetries of the lateral ventricles[16], which should not be considered, per se, as an evidence of cause of epilepsy. As in Case 3, the triggers and spells features in this patient directed the investigation and diagnosis towards syncope. Even the clonic movements presented by the patient should not be confused with epileptic phenomena, since either cardioinhibitory and vasodepressor syncopes, or syncopes of the mixed type may be present with convulsive spells[9]. The seizures secondary to syncopal spells are usually tonic and asymmetric, lasting from three to 30 seconds, mostly around 15 seconds. Finally, Lempert et al.[17] induced syncope in 42 healthy volunteers, 90% of whom experienced myoclonus, usually multifocal. Additional features such as head turning, oral movements, or attempts to sit up occurred in 80%. These motor phenomena are often erroneously considered signs of seizure.

Table 2. Syncope triggers.

Triggers	
Micturiction	Deglutition
Defecation	Cough
Glossopharyngeal neuralgia	Postprandial
Orthostatic	Valsalva manouver
Oculovagal manouver	Sneezing
Venipuncture	Diving
Jacuzzi	Weight-lifting
Trumpet playing	Carotid sinus stimulation
Instrumentation (e.g. small surgical procedures)	Staying inside too ample or crowded places
Drugs	

*modified from Landau[21].

DISCUSSION

Epilepsy and syncope are two conditions with prevalence rates in the general population, of around 1.5 and 3/100, respectively[18,19]. This high prevalence must be considered when first seeing a patient with a history of sudden episodes of loss of consciousness. Diagnosing both conditions is not always clear-cut, but in many cases there are some clinical clues for the diagnosis (Table 1) and/or the report of event triggers (Table 2). Excessive laboratory investigation unnecessarily inflates medical costs[20-22], and, in inexperienced hands complementary investigation often takes precedence, leading to diagnostic confusion.

Fainting is probably the single commonest reason for requesting an EEG, with up to 20% of the

population revealing non-specific abnormalities open to misinterpretation. Therefore, most requests come from non-specialist settings, and many EEGs are reported by neurophysiologists without great experience of epilepsy and its management, with a considerable potential for misdiagnosing faints as seizures[23]. In fact, if syncope is suspected, an EEG is not indicated at first hand since it is likely to reveal normal phenomena or non-specific abnormalities instead of specific epileptiform discharges. External[24] and internal loop recorders[25] have been added more recently to the syncope lab armamentarium and proved to be useful in revealing unexplained cardiogenic syncope, in spite of increasing investigational expenses[26].

Several aspects add complexity to this theme. Probably the most confusing aspect is that seizures may be caused by syncopal attacks. This finding was described in 11.6% of 216 pediatric and adolescent patients with a positive tilt-test[9]. Furthermore, antiepileptic drugs may depress the cardiac conduction or contractile functions[27], and their equivocal use may expose the patient to further cardiovascular symptoms and an increase in the frequency of syncopal episodes might be misinterpreted as a "refractory epilepsy". On the other hand, epileptic seizures may eventually induce cardiac arrest[28], a mechanism not fully excluded for explaining sudden death in epilepsy[29]. Perhaps, selected patients with epilepsy should be evaluated for disorders of cardiac pacing, heart block conduction disorders or myocardial contractile dysfunction.

However, the cases herein described are less complex than some of the issues addressed above, and there are some examples of how easily the physician might be fooled by a first clinical impression. In truth, they may exemplify the say that "there is a short gap between a good doctor and no doctor", since most of patients described above would have benefited from a less aggressive approach to their cases.

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