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Clinical Report

Instability in Patients with CANVAS: Can Computerized Dynamic Posturography Help in Diagnosis?

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OBJECTIVE: To describe the pattern of dynamic posturography or its role in diagnosis in patients with cerebellar ataxia with neuropathy and vestibular arreflexia syndrome (CANVAS).

MATERIALS AND METHODS: We present and describe posturographic data of four patients diagnosed with the CANVAS syndrome in a tertiary hospital.

RESULTS: In all patients, the average balance score was diminished. Two patients presented a pattern of visual dependence. The other two showed misuse of three posturography sensory information (visual, vestibular and propioceptive information), specially null use of vestibular information, deterioration of somatosensory input, and poor use of strategies, particularly in conditions 5 and 6.

CONCLUSIONS: If there is misuse of somatosensory information in sensory organization test (SOT) in a patient with bilateral vestibular deficit, a possibility of CANVAS should be considered. The SOT provides valuable information, because it evaluates sensory inputs influence the maintenance of balance.

KEYWORDS: Cerebellar ataxia, vestibulopathy, neuropathy

INTRODUCTION

In 2004, cerebellar ataxia with bilateral vestibulopathy syndrome was described [1] based on four cases of cerebellar ataxia and bilateral vestibulopathy, three of which also had peripheral sensory neuropathy. In 2011, Szmulewicz et al. [2, 3] presented two broader series of patients, all with the absence of sensory action potentials. This finding made the neuropathy part of the syndrome with the denomination of cerebellar ataxia, neuropathy, and vestibular arreflexia syndrome (CANVAS).

The number of CANVAS cases published currently is not very high, probably because it is an under-diagnosed syndrome. Instability is one of the main symptoms, which can originate from the cerebellar ataxia, bilateral vestibulopathy or neuropathy. The diagnosis of one of the deficits does not necessarily lead to suspicion of a possible association between them in this entity. The diagnostic criteria for CANVAS [4], which establishes four levels of diagnostic safety (CANVAS possible, probable, definitive, and histopathologically definitive), have been recently updated. These criteria are based on data from vestibulo-ocular reflex examinations, cerebellar function tests, neurophysiological tests, exclusion of other causes of ataxia, and if possible, histopathological data.

Instability, an essential symptom, needs evaluation with different balance tests, among which computerized dynamic posturography (CDP) is predominant. CDP allows for quantification of the balance and use of sensory systems directly involved in maintaining stability (proprioceptive, visual, and vestibular). Patients with CANVAS, in addition to cerebellar ataxia, experience alterations in the information provided by these systems; these may be proprioceptive (because of neuronopathy) and vestibular (because of bilateral vestibulopathy). Therefore, CDP initially seems a good test to typify instability in patients with CANVAS. It is striking that the posturographic data are not included in the diagnostic criteria of the syndrome [5].

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Table 1. Demographic and clinical data and vestibular tests of the four patients

Case	Sex	Age	Years since instability onset	Comorbidities	Pure tone audiometry	Other symptoms	Spontaneous nystagmus	Pendular smooth pursuit	Caloric test	vHIT	cVEMPs
1	M	73	9	None	Severe sensorineural bilateral hearing loss at high frequencies	Dysarthria and sweating	Down-beating	Saccadic pursuit	BVA	Low bilateral gain; covert and overt saccades	Normal
2	M	62	4	Migraine	Normal	Dysarthria	Down-beating	Saccadic pursuit	BVA	Absence of collaboration	Normal
3	F	80	3	Arterial hypertension and dyslipidemia	Moderate sensorineural progressive bilateral hearing loss	Paresthesia in legs	Down-beating	Saccadic pursuit	BVA	Low bilateral gain; covert and overt saccades	P1 latency bilaterally delayed
4	M	60	9	Glaucoma	Normal	Dysarthria	Down-beating	Saccadic pursuit	BVA	Low bilateral gain; covert and overt saccades	Right ear P1 latency delayed; left ear normal

vHIT: video head impulse test, cVEMPs: cervical vestibular evoked myogenic potentials, M: male, F: female, BVA: bilateral vestibular arreflexia

This study aimed to discuss the possible existence of posturographic pattern characteristics of patients with CANVAS. If present, it would be useful as a warning sign in patients with bilateral vestibular deficit.

MATERIALS AND METHODS

Design

This retrospective descriptive study was performed in the neurotology unit of an otorhinolaryngology department of a third-level hospital. We present the posturographic data of four patients diagnosed with CANVAS.

Patients

Three males and one female met the diagnostic criteria for definitive CANVAS disease[4]. All of these exhibited cerebellar atrophy upon magnetic resonance imaging and electromyography data of peripheral sensory neuropathy. Genetic tests to exclude Friedreich ataxia and spinocerebellar ataxia 1, 2, 3, 6, 7, 12, 17, and 36 were performed. None of the patients had a familiar history of symptoms suggesting CANVAS. Sex, age at the time of registration, duration of disease, comorbidities, symptoms, presence or absence of hearing loss, and vestibular function assessment are included in Table 1.

The exclusion criteria applied were as follows:

a) Cognitive decline or reduced cultural level that prevents the patient from understanding the examinations
b) Organic diseases that prevent standing, which is necessary to perform CDP
c) Balance disorders caused by diseases other than CANVAS (neurologic, vestibular, locomotor, etc.)

Methods

All patients underwent CDP using the Neurocom® Smart Equitest posturographic platform, NATUS balance and mobility®, USA. The posturography comprises the following:

1. Sensory organization test (SOT): It includes quantification of the patient's displacements from his/her center of gravity in six different sensory information conditions, which are as follows:
   - Condition 1: fixed support, visual surround, and eyes open
   - Condition 2: fixed support and eyes closed
   - Condition 3: fixed support, eyes open, and moving visual surround
   - Condition 4: moving support, eyes open, and fixed visual surround
   - Condition 5: moving support and eyes closed
   - Condition 6: moving support, eyes open, and moving visual surround

   Each of these conditions was repeated consecutively thrice. Each condition is performed for 20 seconds each time.
2. Limits of stability (LOS): Following the visual feedback pictogram, the patient should voluntarily move his/her center of gravity without moving their feet on the posturographic platform to reach eight points around him/her. These points represent 100% of the limit of displacement subject from his/her center of gravity, according to the height and age.

Analysis software

All descriptive statistical analyses were performed using the Statistical Package for the Social Sciences software, version 15 (SPSS Inc., Armonk, NY, USA).

Ethics

Informed consent in accordance with the Declaration of Helsinki was obtained from the four patients included in this study. The study was approved by the ethics committee of the hospital.

RESULTS

Figures 1-4 indicate the SOT results of the four patients. In all patients, the average balance score was diminished, with values much lower than the limit of normality for their age. Two records (1 and 3)

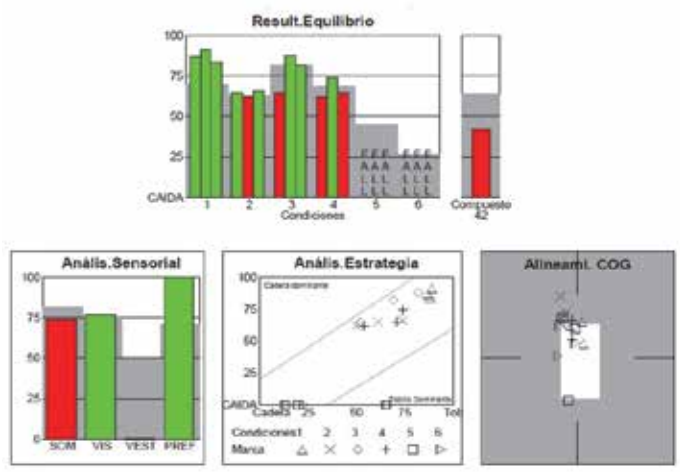

Figure 1. SOT of patient 1. Poor average balance (42%), visual dependence pattern. Result. Equilibrio: balance results. CAIDA: fall. Condiciones: conditions. Compuesto: Composite. Anális Sensorial: Sensory analysis. SOM: somatosensory. VIS: visual. VES: vestibular. PREF: visual preference. Anális. Estrategia: Strategy analysis. Cadera: hip. Tobillo: ankle. Alineami. COG: Center of gravity alignment

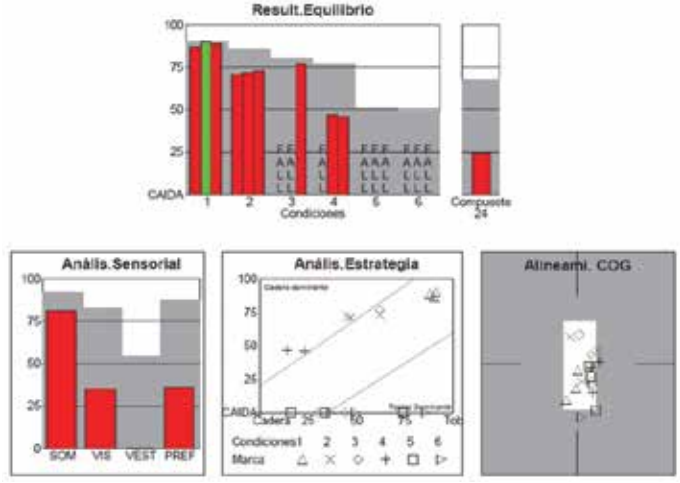

Figure 2. SOT of patient 2. Poor average balance (24%), multisensory deficit pattern

presented a pattern of visual dependence. The other two (2 and 4) showed misuse of the three sensory information (visual, vestibular and propioceptive information). It is noteworthy practically null use of vestibular information, and the deterioration in the somatosensory input in the four patients. All patients presented poor use of strategies, particularly in the most complex sensory conditions (5 and 6), with predominant and inefficient use of the ankle strategy.

Regarding stability limits (Figure 5), there was no pattern common to all four patients, being normal or practically normal in patients 1, 2, and 4 and altered in patient 3 (the oldest). The normality of LOS is striking in the face of severe alteration in SOT.

DISCUSSION

The CANVAS syndrome is equally diagnosed in men and women and can manifest in a wide range of age and mainly in the sixth decade of life. The genetic component has not been conclusively demonstrated. The disease is mainly believed to be of recessive inheritance, al-

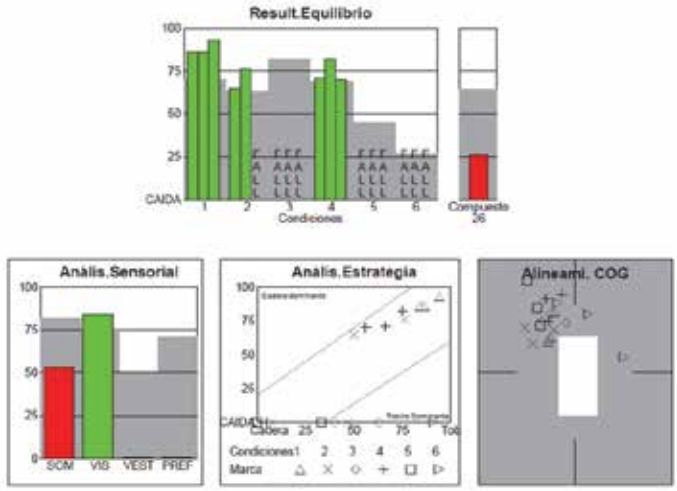

Figure 3. SOT of patient 3. Poor average balance (26%), visual dependence pattern

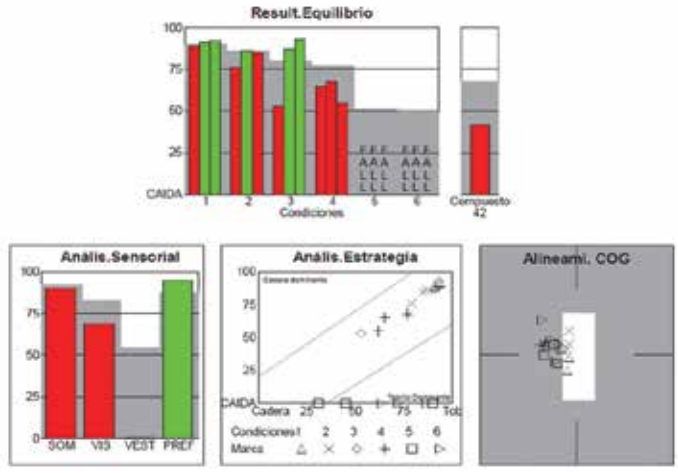

Figure 4. SOT of patient 4. Poor average balance (42%), multisensory deficit pattern

though it has been reported in six pairs of affected siblings, without previous family history. This states the possibility of an autosomal dominant late-onset pattern with incomplete penetrance [2].

In addition to the symptoms of cerebellar atrophy, bilateral vestibular deficit, and neuropathy (mainly sensitive, particularly proprioceptive, and absence of deep tendon reflexes), the presence of autonomic neuropathy (postural hypotension, sweating, etc.) has been described in 91% of the patients with CANVAS [4].

Regarding hearing, two patients presented sensorineural hearing loss, one with severe failure at high frequencies, and one with moderate progressive failure from high to low frequencies. It was noted that in 73 and 80 year-old patients, probably a presbycusis with hearing loss of cochlear origin, associated with age, but without but without having done other tests to prove it in the case study. No relationship was found between bilateral vestibulopathy and sensorineural hearing loss in CANVAS; it should be studied with other tests as brainstem auditory-evoked potentials, in case there is any component of sensory impairment in the auditory nerve in these patients [2, 4].

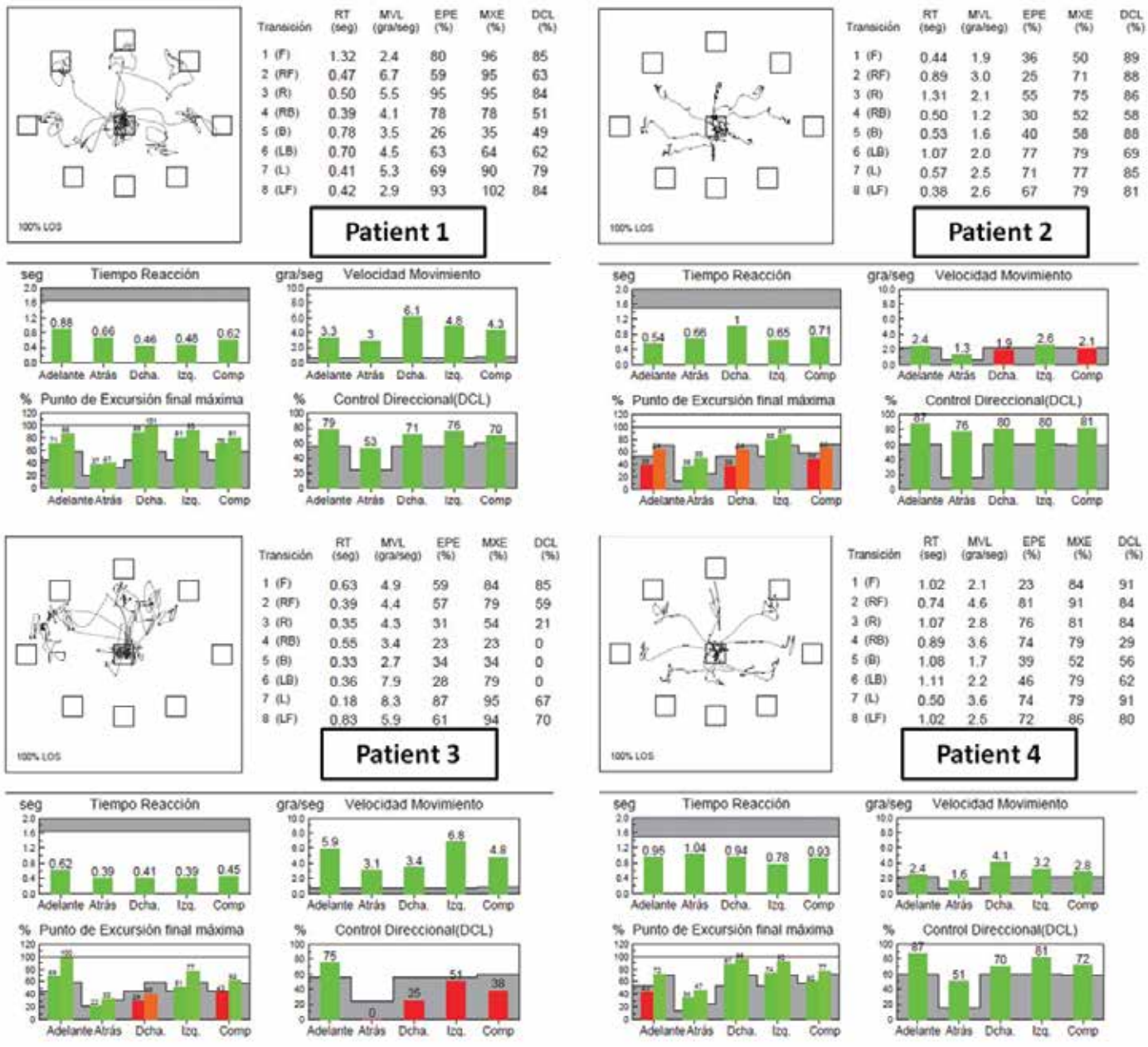

Figure 5. LOS of the four patients. Transición: transition. Tiempo reacción: reaction time. Velocidad movimiento: movement velocity. Punto de excursión final máxima: End and maximum excursion point. Control direccional: directional control

The diagnosis is easy if the clinician is able to suspect this syndrome. It should be ruled out in all patients with severe bilateral vestibulopathy. The instrumental evaluation of the vestibulo-ocular reflex is necessary for diagnosis [4, 6]. A bilateral vestibular deficit not explained by other causes (vestibulotoxicity or bilateral Meniere's disease) always requires screening for CANVAS. Approximately 30% of bilateral vestibular deficits with non-obvious origin may correspond to this syndrome [7].

The almost null existence of publications evaluating balance in these patients with dynamic posturography is surprising. In our patients, as expected, there is a misuse of vestibular (very severe) and proprioceptive inputs. The efficiency in the use of visual information was variable in our patients. This sensory pathway is not altered in patients with CANVAS; nevertheless, it is not efficient (and its score is decreased) in several patients with vestibular lesions. The good or bad use of visual information in CANVAS can be conditioned by the existence of a spontaneous down-beating nystagmus in 65% of the patients, as observed in four of our cases [7]. A misuse of the somatosensory and vestibular inputs is repeated in all patients, which is consistent with the affected sensory pathways.

CONCLUSION

Posturographic studies should be a part of the evaluation of a patient with instability of any origin. If there is misuse of somatosensory information in the SOT in a patient with bilateral vestibular deficit, the possibility of CANVAS should be considered. Less utility seems to

have the quantification of stability limits. The SOT provides valuable information, because it evaluates sensory inputs that influence the maintenance of balance.

Ethics Committee Approval: The protocol has been approved by the Independent Ethics Committee of Galicia (No: 2014/411).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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