Canvas: A case report

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Abstract

CANVAS is an acronym for cerebellar ataxia, neuropathy and vestibular areflexia syndrome that was recently described in 2011. This paper reports a case of a 69 years old female that presented a history of dizziness for 9 years, associated with altered vestibulo-ocular reflex (VVOR) and bilateral hypofunctiom at video head impulse test (vHIT), wicth confirmed CANVA syndrome. Imbalance is a consistent symptom of CANVAS and, in most cases, it is the first to manifest. Its presentation demonstrates the importance of the specialist's need for knowledge of this clinical condition to enable an assertive diagnosis.

Keywords: CANVAS; Vestibular areflexia; Vídeo head impulse test; Vestibulo-ocular reflex; Dizziness; Vestibulo hypofunction.

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Introduction

CANVAS, an acronym for cerebellar ataxia, neuropathy and vestibular areflexia syndrome, was first described in 2011 by Szmulewicz and collegues, who also proposed the diagnostic criteria for CANVAS in 2016. The most important findings are: clinical evidence of bilateral vestibular hypofunction, clinical evidence of cerebellar impairment (cerebellar atrophy on magnet resonance image (MRI) and/or signs of cerebellar impairment on examination), and abnormal nerve conduction testing that is consistent with a sensory deficit but excludes nerve entrapment neuropathies or other known pathology (neurophysiologic evidence of a neuronopathy (ganglionopathy).[1,2]

Most cases of CANVAS are diagnosed on an outpatient basis, as the characteristic clinical sign, altered vestibulo-ocular reflex (VVOR – visually enhanced vestibulo-ocular reflex), is simple to be identified in the office and recorded by video-oculography.[1] It can only be obtained if both smooth-pursuit eye movements and the vestibulo-ocular reflex are deficient. In addition to this manifestation, patients with this syndrome have sensory deficits on nerve conduction studies as evidenced by abscent or reduced sensory nerve action potentials (SNAPS), in addition to central changes such as cerebellar atrophy, which involves the cerebellar vermis and lateral hemispheric atrophy (consistent pattern of anterior and dorsal vermis atrophy, the latter involving vermal lobules VI, VIIa, and VIIb. Laterally, a pattern of hemispheric atrophy predominantly affecting crus I (corresponding to vermal lobule VII) was seen),[3] identified through MRI of the skull.[4]

The genetic disorder in CANVAS was discovered to be an abnormal biallelic expansion in the replication factor C subunit 1 (RFC1), an autosomal recessive inherited disease.[5,6]This pathological expansion was found in 100% of the familial form, and 92% of seemimgly sporadic ones when the triad was complete.[7] This mutation has been identified as a major cause of late-onset ataxia, which affects the cerebellum, sensory ganglia including the vestibular system, and explaining the pathology of CANVAS.[5,8]

Case report

DLSS, 69 years old, female, started with dizziness in 2012, previously diagnosed with PPPD (persistent perceptual postural dizziness), due to the dizzying condition associated with great emotional stress, provoked by the death of her mother.

Only in 2020 the diagnosis of CANVAS was confirmed after dizziness recurrence, when the patient sought a specialized service in otorhinolaryngology.

She reported unspecific dizziness with imbalance and light headness whenever she was standing. She also had sensorineural hearing loss in both ears (presbycusis), without tinnitus. On physical examination, bilateral corrective saccade to the head impulse test (HIT) was observed and difficulty in performing the Romberg and Fukuda test.

After initial evaluation, complementary exams were requested. The video head impulse test (vHIT) revealed bilateral hypofunctiom (Figure 1), the visually enhanced VVOR was also abnormal (Figures 2 and 3) and posturography revealed changes in the static balance and in the integration of the balance systems (somatosensory, vestibular and visual) (Figure 4). These tests were all performed in a specialized clinic.

After the results of the complementary exams, which confirmed bilateral labyrinth hypofunction, the patient was referred to a neurologist for evaluation of neuropathy and cerebellar ataxia. After physical examination, the speciallist confirmed the cerebelar ataxia, that demonstrated pendular patellar reflex, finger-nose dysmetria, normal elevation of limbs with eyes closed and gait with extended steps (drunken gait), complemented by the aid of an electroneuromyography examination of the upper and lower limbs (ENM), with axonal degeneration. Then, magnetic resonance imaging (MRI) was requested, which showed cerebellar atrophy.

At the moment, the patient has been in vestibular rehabilitation for 3 months, with improvement of vestibular symptoms.

Figure 1. Video Head Impulse Test showing hypofunction of all semicircular canals in both ears

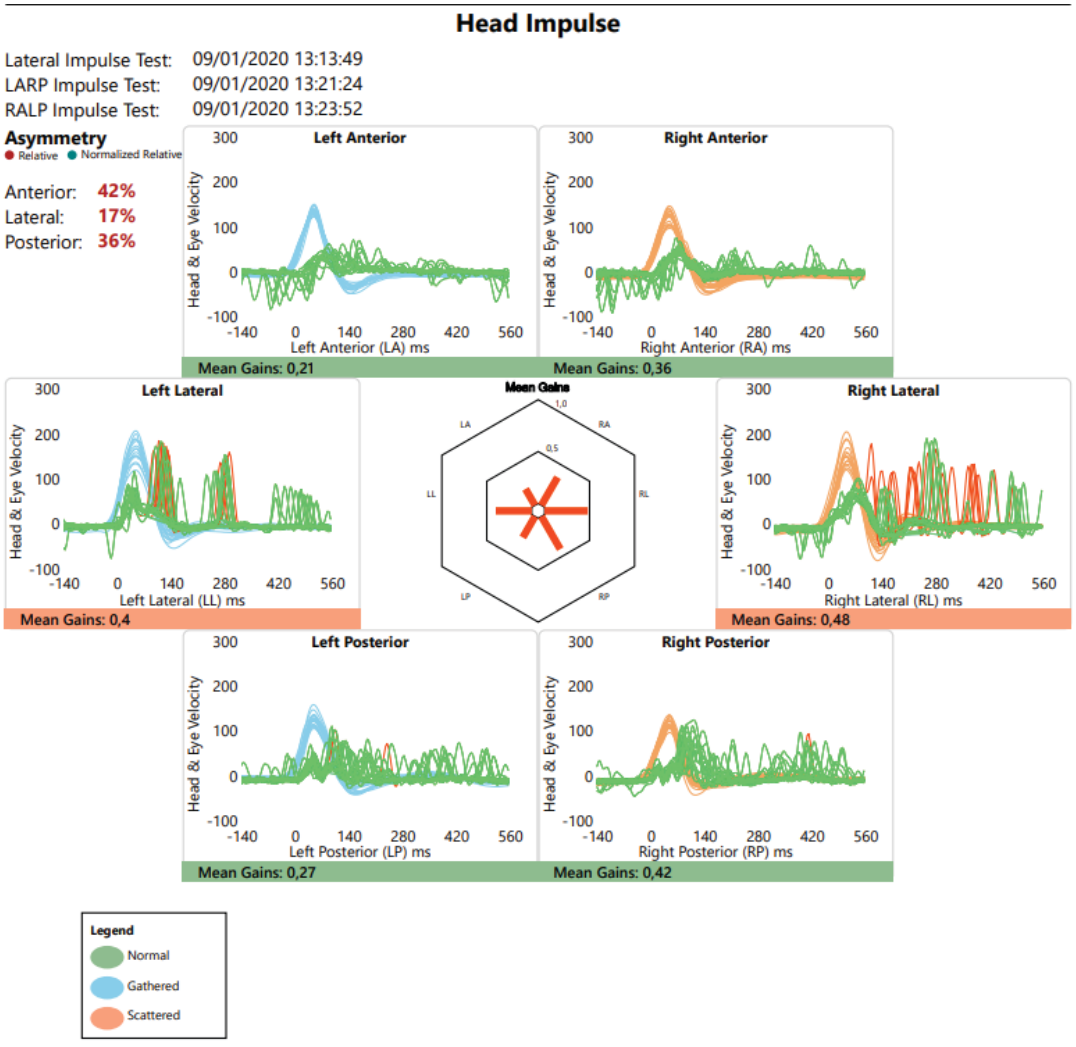


Figure 2. refixation balances during horizontal rotation of Altered visually enhanced vestibulo-ocular reflex (VVOR): the head at approximately 1 Hz

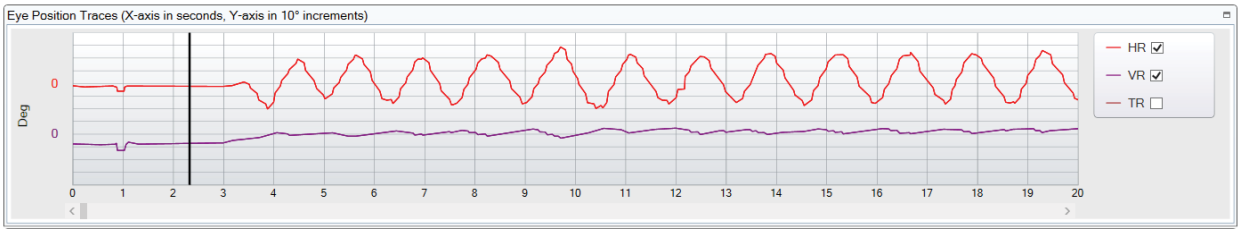


Figure 3. Altered visually enhanced vestibulo-ocular reflex (VVOR): refixation balances during horizontal rotation of the head at approximately 1 Hz

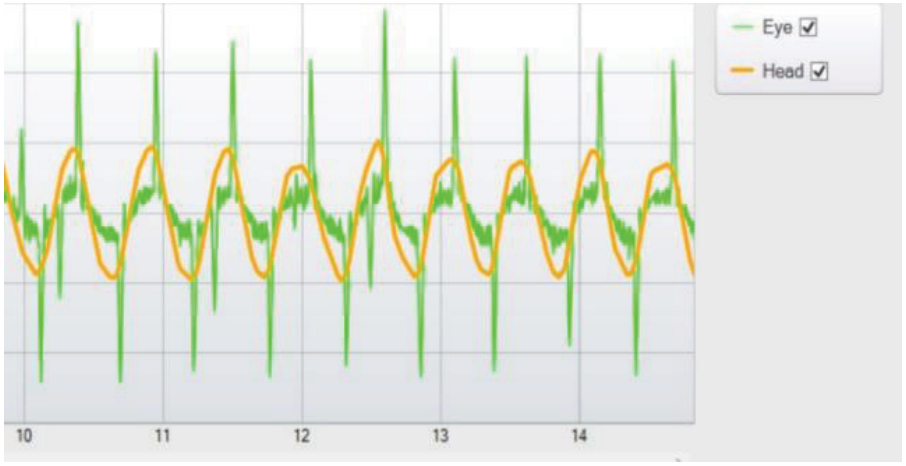
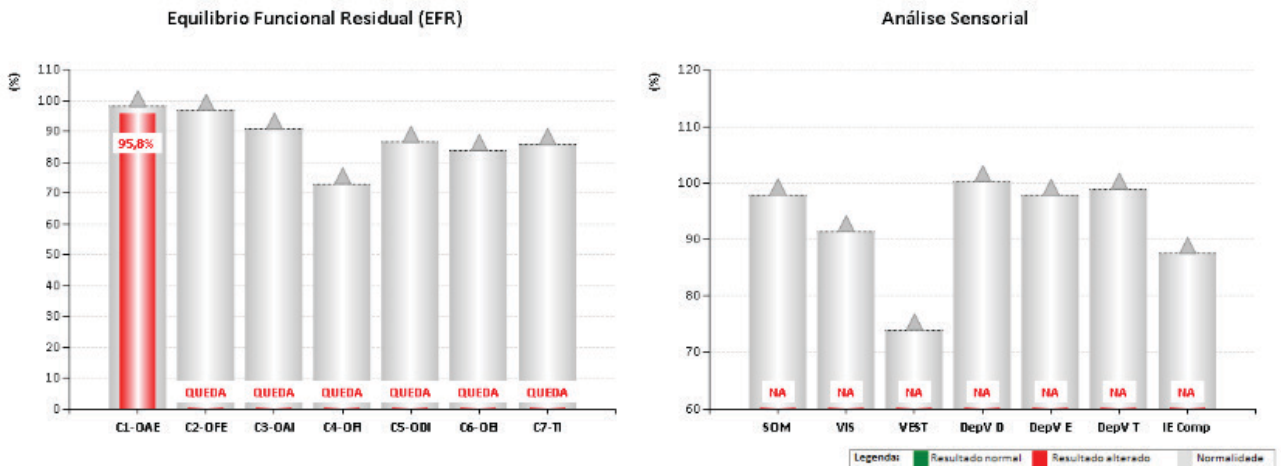


Figure 4. Posturography showing alteration in the integration of all pathways of balance (somatosensory, visual and vestibular)



Discussion

Vestibular areflexia and sensory loss in CANVAS syndrome have been attributed to a sensory neuronopathy that affects the dorsal root and V, VII, and VIII cranial nerve ganglia. Histopathological studies of the temporal bone in post-mortem patients showed severe impairment of Scarpa's ganglion with a reduction in the number of ganglion cells bilaterally as a consequence, bilateral vestibular nerves were also atrophied, as they originated in the ganglion in question[9,10]

The auditory component of the vestibular nerve was intact, in post-mortem analysis, with the vestibular terminal organs (ridges and macules) unchanged.[10] Unexpectedly, the facial nerves may be atrophied, especially in the geniculate ganglion, in addition to the altered trigeminal ganglion with an important decrease in the cellular component. The neuropathology of these patients shows loss of Purkinje cells (predominantly in the vermis and lateral cerebellum)[9]

Imbalance is a consistent symptom of CANVAS and, in most cases, it is the first to manifest, although sometimes it develops as the syndrome progresses.[1] The characteristic oculomotor sign of this syndrome is the clinical evidence of an abnormal visually enhanced VVOR. The VVOR assessment is done by demonstrating clinically the presence of compensatory rather than smooth saccadic eye movements, moving the head from side to side while the patient looks at a fixed target, and represents combined cerebelar and bilateral vestibular impairment.[1,11] The opticokinetic reflex occurs when, in the presence of an entire scene that oscillates from side to side, different from the small target in the smooth search, compensatory eye movements are produced to fix the image on the retina.[12]

A diagnostic challenge is to make sure that a patient who has one of the CANVAS triad (cerebelar ataxia, bilateral vestibulopathy and a somatosensory deficit) has also a second, or, indeed, a third component.

There are some differential diagnoses for CANVAS, the most important include: spinocerebellar ataxia (SCA3), multiple system atrophy with predominant cerebellar ataxia (MSAc), idiopathic cerebellar ataxia and bilateral vestibulopathy (iCABV), and Wernecke's encephalopathy.[13]

The case report fulfills all the criteria of the syndrome, with proof through complementary exams. Both VHIT and VVOR show bilateral labyrinthic areflexia (Figures 1, 2 and 3), posturography (Figure 4) with changes in all balance systems (visual, somatosensory and vestibular), ENM with axial degeneration, physical examination compatible with cerebellar ataxia and sensory deficit, in addition to skull MRI which shows cerebellar atrophy. As the patient in question does not have the RFC1 gene test positive or at least the SCA3 gene test negative, therefore we can affirm that it is highly suspisious for CANVAS.

Conclusion

In recent years much has been studied about CANVAS, including its clinical manifestations, diagnostic and histopathological criteria.[2,10,11] Despite this, it is still a little known syndrome in medical practice. Its presentation, associated with otorhinolaryngological signs and symptoms, demonstrates the importance of the specialist's need for knowledge of this clinical condition to enable an assertive diagnosis

The follow up by the neurologist and otorhinolaryngologist is to control vestibular symptoms by vestibular rehabilitation. The prognosis of the CANVAS is still reserved, studies are needed to better elucidate the clinical management.

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