LETTER TO THE EDITOR

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Sensory Neuronopathy in CANVAS: Cerebellar Ataxia, Neuropathy, and Vestibular Areflexia

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The association of cerebellar ataxia, neuropathy and vestibular areflexia (CANVAS) constitutes a syndrome of degenerative aetiology and relentless progression.[1,2] Usually sporadic, it has occasionally been found in siblings, raising the possibility of recessive transmission.[1] Both the neuromuscular manifestations and the clinical diagnosis of CANVAS could benefit from better definition; as a result, the aim of this work has been to review them in a patient with this disease.

A 76-year-old man presented 21 years ago with unsteadiness of gait that worsened in the dark and gradually progressed to impair independent walking for the past 7 years; oscillopsia and dysarthria were also reported by the patient. A neurological examination revealed absent ankle reflexes, wide-based stance, a positive Romberg sign, and a markedly ataxic gait that required bilateral support. Plantar responses were flexor. Vibration sense was absent distal to the iliac crests, diminished distal to the clavicles, and normal in the face; finger and toe position sense was impaired; and pain, thermal, and light touch sensation was preserved. Dysmetria, decomposition of movement, and final tremor of the extremities were found, as was horizontal gaze-evoked nystagmus. The horizontal head impulse test (Halmagyi manoeuvre) showed correction of eye position with saccadic movements bilaterally.

Among the complementary tests, bilateral, bithermal caloric vestibular stimulation induced small erratic eye movements on videonystagmography, without eliciting any physiological oculomotor response.

An electrophysiological study revealed an absence of sensory potentials in the nerves of the extremities, and compound muscle action potentials (CMAP) of low amplitude after stimulation of both facial nerves. A blink reflex demonstrated delayed right R1 (15 ms, normal $\leq$12.9 ms) and ipsilateral R2 (44.2 ms, normal $\leq$40 ms) responses, and a left contralateral R2 response of 44.3 ms (normal $\leq$40 ms).

Motor nerve conduction velocities were normal; electromyographic records of the left tibialis anterior and biceps brachii showed CMAPs of normal amplitude and duration as well as interferential patterns of recruitment on maximal effort.

A study of somesthetic potentials revealed that stimulation of median and tibial nerves did not elicit reproducible responses at the cerebral cortex. Brainstem-evoked auditory potentials showed well-defined responses bilaterally, with normal central conduction times.

A cranial magnetic resonance imaging (MRI) scan showed generalized cerebellar atrophy, especially in the anterior vermis, whereas tractography demonstrated normal pyramidal tracts and middle cerebellar peduncles. The membranous labyrinth did not show any alteration, and an MRI scan displayed a normal spinal cord.

Dynamic mutations of spinocerebellar ataxias 1, 2, 3, 6, and 7; Friedreich's ataxia (FRDA), and fragile X–associated tremor/ataxia syndrome were excluded. Serum determinations of alpha-fetoprotein and carcinoembryonic antigen were normal; blood anti-GAD; endomysial; peroxidase; Hu, Yo, Ri, and Tr antibodies; and titrations for Brucella, syphilis, and *Borrelia burgdorferi* antibodies in serum and cerebrospinal fluid were all negative.

Before the definition of CANVAS in 2011,[1,2] the association of cerebellar ataxia with vestibulopathy and the existence of episodic vestibulocerebellar ataxia were already known.

The clinical complexity of CANVAS, which includes cerebellar ataxia, neuropathy (recently categorized as a sensory neuronopathy[3]), and vestibular areflexia,[1] means that its manifestations have to be systematically looked for, to arrive at a correct diagnosis.

In this patient, cerebellar involvement was expressed by gait ataxia, dysmetria of the extremities, wide-based stance, scanning dysarthria, and atrophy of the cerebellum on MRI. A pure sensory syndrome with a peculiar distribution was evident on examination, as referred to previously: its topography did not suggest a dying-back axonal degeneration, but rather a spinal cord compression, which was ruled out by a normal spinal MRI. Vestibular areflexia was demonstrated in this case by: (1) an abnormal response to caloric vestibular stimulation, which did not elicit a conjugate eye deviation; and (2) an abnormal response to the head impulse test, which showed correction of eye position with saccadic movements, instead of keeping gaze fixed during the manoeuvre.[1]

The demonstration of vestibular areflexia is an essential requirement in the diagnosis of CANVAS. In this case, the abnormal responses to caloric vestibular stimulation and to the head impulse test indicated a severe bilateral vestibular dysfunction and confirmed the diagnosis of this syndrome, distinguishing it from other diseases that associate cerebellar ataxia with a sensory neuronopathy, such as FRDA.

Peripheral nervous system involvement in CANVAS was formerly defined as a sensory, motor, axonal or mixed polyneuropathy,[1,2] albeit it has been identified as a sensory neuronopathy.[3] In this patient, an absence of sensory action potentials in the nerves of the extremities, together with a lack of sensory evoked cortical responses after stimulation of the median and tibial nerves, in combination with a normal electrophysiological exploration of the motor system, pointed to an exclusive involvement of the sensory nervous system, consistent with a neuronopathy affecting the neurons of the dorsal root ganglia.[4]

The low amplitude of CMAPs after stimulation of the facial nerves, and the alterations in the blink reflex found in this case, could be caused by an asymmetrical atrophy of these nerves in their petrous portion, a pathological finding described in CANVAS.[5]

The differential diagnosis of CANVAS must be mainly carried out with FRDA, spinocerebellar ataxias 3, multisystem atrophy with cerebellar involvement, and Wernicke's encephalopathy, which were ruled out in this case by the appropriate clinical, genetic and imaging tests. Episodic ataxia type 4 (periodic vestibulocerebellar

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ataxia) should also be considered, even though this patient did not experience fluctuations in the intensity of ataxia, or episodes of dizziness; other ataxias caused by toxic, paraneoplastic, or autoimmune aetiologies were discarded by the complementary examinations enumerated previously.

To summarize, the demonstration of vestibular areflexia was crucial to establish a diagnosis of CANVAS in this patient. In addition, extensive electrophysiological studies determined that a sensory neuronopathy caused the vibratory hypoesthesia found in this case, caused by injury to the dorsal root ganglia neurons, as recently demonstrated pathologically by Szmulewicz et al.[3] Further research is needed to increase awareness of CANVAS among the medical population and to improve knowledge about the neuromuscular manifestations in this disease.

Disclosures

The authors declare that they have no competing interests.

José Gazulla
Department of Neurology, Hospital Universitario Miguel Servet
Zaragoza, Spain (JG)

María Jesús Pablo-Zaro
Department of Clinical Neurophysiology, Hospital San Jorge
Huesca, Spain (MJP-Z)

Jesús Fraile-Rodrigo
Department of Otolaryngology,
Hospital Universitario Miguel Servet
Zaragoza, Spain (JFR)

Pilar Larrodé
Department of Neurology,
Hospital Clínico Universitario Lozano Blesa
Zaragoza, Spain (PL)

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