

Syndrome of cerebellar ataxia, neuropathy and vestibular areflexia: Diagnosis by caloric vestibular stimulation[☆]

Síndrome de ataxia cerebelosa, arreflexia vestibular y neuropatía: diagnóstico mediante estimulación vestibular calórica

Dear Editor:

Cerebellar ataxia, neuropathy and vestibular areflexia syndrome (CANVAS) is a recently-described progressive degenerative disease whose exact prevalence remains unknown. This syndrome appears mainly sporadically and occasionally affects siblings. This has led researchers to consider the possibility of a recessive inheritance pattern, but the disease has not yet been linked to changes at a specific locus.^{1,2} According to published cases, age at onset ranges from 33 to 71 years; after 10 years with the disease, most patients require support when walking.²

We present the case of a 74-year-old man who for 21 years had experienced gait instability exacerbated by darkness, and diminished foot sensation, which progressively increased until he became unable to walk unaided 5 years ago. Neurological examination revealed absent Achilles reflexes, wide-based stance, positive results on the Romberg test, and markedly ataxic gait requiring bilateral support. Vibratory sensation was abolished below the iliac crests, diminished above that level, and normal in the face; algesia was preserved. The patient presented dysmetria, movement decomposition with essential tremor, scanning dysarthria, saccadic movements during eye tracking, horizontal and vertical gaze-evoked nystagmus, and refixation saccade in the horizontal plane during the Halmagyi head thrust manoeuvre.

Among complementary data, videonystagmography (VNG) showed horizontal spontaneous pendulum movements in the primary gaze position and eye tracking consisting of saccadic movements. Bilateral caloric stimulation induced only small erratic eye movements and the audiometry test showed normal hearing.

The brain MRI revealed cerebellar global atrophy, especially in the superior part of the vermis, with crus I impairment; the membranous labyrinths showed no changes. MR imaging showed normal spinal cord morphology, size, and signal.

An electroneurography study revealed absence of sensory nerve action potentials, as well as normal motor conduction velocity and normal motor unit action potential amplitudes in the nerves in all 4 limbs.

Dynamic mutations of spinocerebellar ataxia (SCA) types 1, 2, 3, 6, and 7, Friedreich ataxia (FRDA), and fragile

X-associated tremor/ataxia syndrome were all excluded. Antigen and alpha-fetoprotein levels were normal; tests for anti-GAD antibodies, endomysium, peroxidase, anti-Hu, anti-Yo, anti-Ri, and anti-Tr antibodies, as well as tests for *Brucella*, syphilis, and *Borrelia burgdorferi* in serum and cerebrospinal fluid yielded negative results.

Before CANVAS was described, researchers were already aware of the association between cerebellar ataxia and bilateral vestibulopathy,³ the presence of peripheral neuropathy in cases of vestibulopathy,^{4,5} and the presence of periodic vestibulocerebellar ataxia.⁶

In this case, cerebellar impairment presented with ataxic gait, limb dysmetria, wide-based stance, and scanning dysarthria. Achilles tendon areflexia was useful for detecting sensory neuropathy (confirmed by electroneurography). While topography may have suggested spinal cord disease, that entity was ruled out by MRI.

Vestibular hypofunction was suspected when doctors performed the head thrust test, which resulted in saccadic movements to refixate,⁷ rather than the eyes maintaining fixation during the manoeuvre. In addition, caloric stimulation generated a very anomalous oculomotor response instead of the typical response (consisting of horizontal nystagmus in the direction of the quick component in response to heat or in the opposite direction in response to cold). This finding confirmed the presence of bilateral vestibular hypofunction.^{8,9}

Vestibular areflexia in CANVAS is caused by neural loss in Scarpa's ganglion, which was described in the only autopsy in the literature.¹⁰ In contrast, vestibular organs remained intact¹⁰ according to the head MRI.

Findings from this study coincide with those described for CANVAS cases; however, subsequent studies are needed in order to better define this syndrome. Meanwhile, we believe that tests of vestibular function in ataxic patients lacking a precise diagnosis may be helpful for detecting cases with vestibulocerebellar impairment.

Acknowledgements

We would like to thank María Jesús Pablo Zaro, Department of Clinical Neurophysiology, Hospital San Jorge, Huesca; Ana Carmen Vela, Department of Radiology, Hospital Universitario Miguel Servet, Zaragoza; and Pilar Larrodé, Department of Neurology, Hospital Clínico Universitario Lozano Blesa, Zaragoza.

References

1. Szmulewicz DJ, Waterston JA, Halmagyi GM, Mossman S, Chancellor AM, Mclean CA, et al. Sensory neuropathy as part of the cerebellar ataxia neuropathy vestibular areflexia syndrome. *Neurology*. 2011;76:1903–10.
2. Szmulewicz DJ, Waterston JA, Macdougall HG, Mossman S, Chancellor AM, Mclean CA, et al. Cerebellar ataxia, neuropathy, vestibular areflexia syndrome (CANVAS): a review of the clinical features and video-oculographic diagnosis. *Ann N Y Acad Sci*. 2011;1233:139–47.
3. Migliaccio AA, Halmagyi GM, McGarvie LA, Cremer PD. Cerebellar ataxia with bilateral vestibulopathy: description

[☆] Please cite this article as: Crespo-Burillo JA, Hernando-Quintana N, Fraile-Rodrigo J, Gazulla J. Síndrome de ataxia cerebelosa, arreflexia vestibular y neuropatía: diagnóstico mediante estimulación vestibular calórica. *Neurología*. 2013;28:591–592.

- of a syndrome and its characteristic clinical sign. *Brain*. 2004;127:280–93.
4. Zingler VC, Cnyrim C, Jahn K, Weintz E, Fernbacher J, Frenzel C, et al. Causative factors and epidemiology of bilateral vestibulopathy in 255 patients. *Ann Neurol*. 2007;61:524–32.
 5. Wagner JN, Glaser M, Brandt T, Strupp M. Downbeat nystagmus: aetiology and comorbidity in 117 patients. *J Neurol Neurosurg Psychiatry*. 2008;79:672–7.
 6. Jen JC. Hereditary episodic ataxias. *Ann N Y Acad Sci*. 2008;1142:250–3.
 7. Halmagyi GM, Curthoys IS. A clinical sign of canal paresis. *Arch Neurol*. 1988;45:737–9.
 8. Baloh RW, Honrubia V, Yee RD, Hess K. Changes in the human vestibulo-ocular reflex after loss of peripheral sensitivity. *Ann Neurol*. 1984;16:222–8.
 9. Baloh RW, Jacobson K, Honrubia V. Idiopathic bilateral vestibulopathy. *Neurology*. 1989;39:272–5.
 10. Szmulewicz DJ, Merchant SN, Halmagyi GM. Cerebellar ataxia with neuropathy and bilateral vestibular areflexia syndrome: a histopathologic case report. *Otol Neurotol*. 2011;32:e63–5.
- J.A. Crespo-Burillo^{a,*}, N. Hernando-Quintana^a,
J. Fraile-Rodrigo^b, J. Gazulla^a
- ^a *Servicio de Neurología, Hospital Universitario Miguel Servet, Zaragoza, Spain*
^b *Servicio de Otorrinolaringología, Hospital Universitario Miguel Servet, Zaragoza, Spain*
- * Corresponding author.
E-mail address: josanjose@hotmail.com
(J.A. Crespo-Burillo).
2 March 2012 7 June 2012

The link between tics and streptococcal infection: A case report[☆]

Relación entre tics e infección estreptocócica: a propósito de un caso

Dear Editor:

Tics are repetitive, stereotyped movements that may be suppressed voluntarily. Patients feel the need to perform them as a means of relieving a mental or physical sensation that precedes them¹; the most frequent cause is Tourette syndrome (TS).² Researchers have tried to establish a link between tics and infection with Group A β -haemolytic streptococcus (GABHS).³ With this in mind, we present the case of a tic arising years after the patient had experienced Sydenham chorea (SC), a condition associated with GABHS, and we discuss the relationship between those episodes.

The patient was a 9-year-old girl who had experienced acute predominantly right-sided chorea, preceded by changes in handwriting and scholastic achievement. Anti-streptolysin antibody (ASLO) titre 1152; echocardiography showing mild mitral regurgitation; normal brain MRI; normal ceruloplasmin; and normal metabolic and hormonal studies. After being diagnosed with SC, she was treated with haloperidol, which improved symptoms, but the chorea persisted during 2 years. Since that time, she has received monthly prophylactic treatment with penicillin G. At the age of 13, she reported motor disorder in the form of brusque dorsal flexion of the left ankle when walking, causing the joint to click. This event could be prevented voluntarily, although the patient felt inclined to provoke it in order to relieve a feeling of tension in that joint. Traumatology study yielded normal results. ASLO: 285 (similar to previous studies); pharyngeal exudate presented normal

flora. Symptoms resolved spontaneously in 1 year without treatment.

The role played by GABHS in tic aetiopathogenesis is a topic of debate. Tics are known to be movement disorders that are frequently associated with streptococcal infection; on some occasions, they meet diagnostic criteria for TS.³ Nevertheless, the nature of this association is unclear.⁴ For example, we know that GABHS may provoke SC, which is the neurological autoimmune manifestation of rheumatic fever; it presents with chorea and other neuropsychiatric symptoms⁵ and tics in some cases.^{5,6} The same autoimmune mechanism may be involved in both syndromes. In fact, patients with SC have been described as being more susceptible to drug-induced tics than other patients.⁷ Doctors have also indicated that children with a prior history of tics are more likely to develop Sydenham chorea.⁸ In this sense, the autoimmune nature of this association between entities is reinforced by the concomitant finding of specific anti-basal ganglia antibodies and high ASLO titres in patients with TS.⁹ Lastly, another argument supporting the presence of an autoimmune aetiopathogenic link between tics and streptococcal infection is the description of paediatric autoimmune neuropsychiatric disorder associated with streptococcal infections (PANDA). This disorder is defined by relapsing-remitting episodes of tics and/or obsessive-compulsive disorder associated with a recent streptococcal infection and attributed to an autoimmune mechanism,¹⁰ although whether or not it really exists is currently a very controversial topic.¹¹

In our case, the motor disorder described by the patient met clinical criteria for a tic, and was interpreted as a simple motor tic of the foot during walking. Such tics, while less frequent than others, have been described in the literature.¹² Therefore, the presence of SC and tics in the same patient suggests yet again the possibility of a link between tics and streptococcal infection; the novel finding in our case is that the tic appeared years after SC. This being the case, our patient may have developed an increased propensity for tics after having SC. This would probably have been caused by the presence of circulating anti-basal ganglia antibodies. The possibility of there being

[☆] Please cite this article as: Peña Llamas E. Relación entre tics e infección estreptocócica: a propósito de un caso. *Neurología*. 2013;28:592–593.