P112

CAWEDD (Cerebellar Ataxia With Evidence of Dopaminergic Deficit): CANVAS is the last on the list

Andrea Mignarri[1], S. Locci, E. Belli, A. Tessa, N. De Stefano, E. Tardelli, S. Sestini, F.M. Santorelli, R. Ceravolo

[1]Department of Medical, Surgical and Neurological Sciences, Unit of Neurology and Neurometabolic Diseases, University of Siena, Siena, Italy
[2]Department of Medical Specialties, Unit of Neurology, University of Pisa – Santa Chiara Hospital, Pisa, Italy
[3]Unit of Molecular Medicine, IRCCS Stella Maris, Pisa, Italy
[4]Unit of Nuclear Medicine, Department of Diagnostic Imaging, N.O.P. - S. Stefano, U.S.L. Toscana Centro, Prato, Italy

Introduction: Cerebellar Ataxia, Neuropathy and Vestibular Areflexia Syndrome (CANVAS) is caused by biallelic intronic AAGGG repeat expansions in the *RFC1* gene, and is the major cause of late-onset hereditary ataxia. *RFC1* expansions are also responsible for a significant percentage of "idiopathic" sensory neuropathy, without ataxia. Nigrostriatal degeneration at [123I]-FP-CIT is a typical finding of MSA-C, but has also been reported in a number of hereditary ataxias such as SCA2, 3, 6, 17, 31, SPG7, and AOA1, with or without parkinsonism. Interestingly, biallelic *RFC1* expansion has been reported in patients with Parkinson's disease and without ataxia as well as in cases with MSA-C.

Objective: We present two patients with CANVAS who showed DAT evidence of nigrostriatal degeneration. The aim is to provide further evidence of dopaminergic deficit in hereditary cerebellar ataxias, by adding to the list the one thought to be the most frequent.

Methods: We performed clinical evaluation, ENG/EMG, brain MRI, [123I]-FP-CIT, and genetic investigation of *RFC1* expanded alleles.

Results: Both patients carried biallelic intronic AAGGG repeat expansions in *RFC1* and showed slowly progressive ataxia associated with cerebellar atrophy and axonal sensory neuropathy. Interestingly, [123I]-FP-CIT revealed nigrostriatal degeneration despite the absence of parkinsonism.

Discussion: CANVAS represents the latest member of a large group of pathologies grouped under the umbrella of CAWEDD (Cerebellar Ataxia With Evidence of Dopaminergic Deficit). The pathophysiological mechanisms underlying loss of dopaminergic neurons in cerebellar ataxia is not clear. Intriguingly, cerebellar dysfunction seems to be protective towards parkinsonism despite presence of nigrostriatal denervation: subthalamic nucleus lesion, observed in SCA2 and SCA3, may counteract the effects of the nigrostriatal depletion and therefore explain the lack of clinical parkinsonism; however, disruption of the cerebellum may be itself the principal mechanism preventing and/or compensating the motor effects of striatal denervation in patients with ataxia. We suggest to consider *RFC1*-related diseases in late onset cases where ataxia combines with [123I]-FP-CIT abnormalities.