SCA3 in Italy: time to change mind

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Introduction: Spinocerebellar ataxia type 3 (SCA3), also known as Machado-Joseph disease (MIM, 607047), is a neurodegenerative disorder characterized by a ataxia, ophthalmoplegia, peripheral neuropathy, pyramidal and extrapyramidal disorders, caused by an expanded CAG/CTG repeat in the coding region of *ATXN3*. SCA3 is usually considered absent in Italy. Herein we describe a short series of patients , which somewhat challenges such an opinion.

Materials, methods and results:

Patient 1 and 2

•54-year-old man of Umbrian ancestry with progressive unsteady gait since age 47.
•Ataxic gait, mild dysmetria and dysdiadochokinesia as well as bilateral fixation nystagmus and saccadic pursuit, moderate dysarthria
•SARA score 27.5/100
•No pyramidal, extrapyramidal signs nor mental retardation.
•Facial fasciculations
•NCS/EMG:motor axonal neuropathy
•MRI showed moderate pancerebellar atrophy.
•His 50-year-old sister was similarly affected since age (SARA 20/100). Interestingly, both patients showed pseudo-exophthalmos, which is considered specific of SCA3.
•*ATXN3* : heterozygous CAG expansion (CAG number 73 ±3 in both patients). No other SCA genes showed expanded CAG tracts.

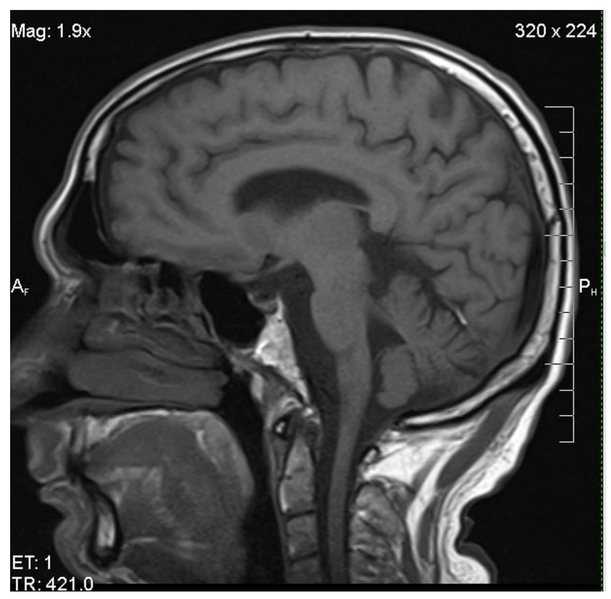
Patient 3

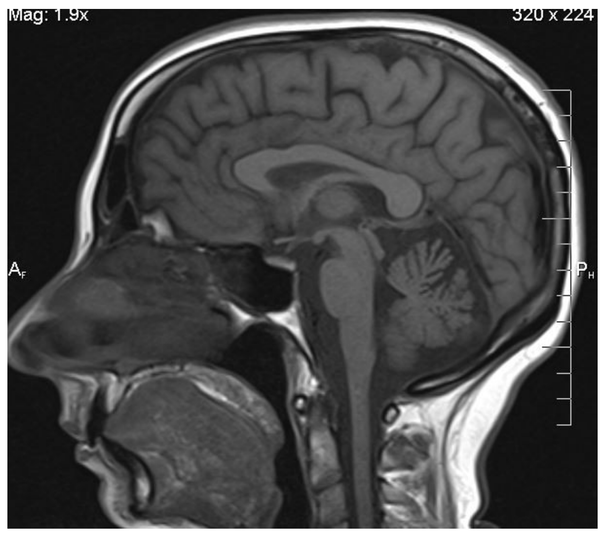
•65-year-old man with unsteady gait since age 55.
•Gait ataxia, horizontal and vertical ophthalmoparesis, mild dysarthria, dysphagia, dysmetria and dysdiadochokinesia.
•Except for a bilateral extensor plantar, no pyramidal signs. NCS/EMG: sensory axonal neuropathy
•MRI : mild cerebellar atrophy
•*ATXN3:* heterozygous CAG expansion (CAG number >55).

•***Patient 4***

•26-year-old Han Chinese man. His family originated in the Shanghai region and includes at least other 6 affected relatives with a clear-cut autosomal dominant inheritance.
•Onset at 20 years.
•Marked ataxic changes were found in gait and both upper and lower limbs. Dysphagia and speech changes were reported by his relatives. Marked diffuse spasticity and brisk tendon reflexes were also noted as well as facial fasciculations.
•*ATXN3:* heterozygous CAG expansion (CAG number 75 ±3).

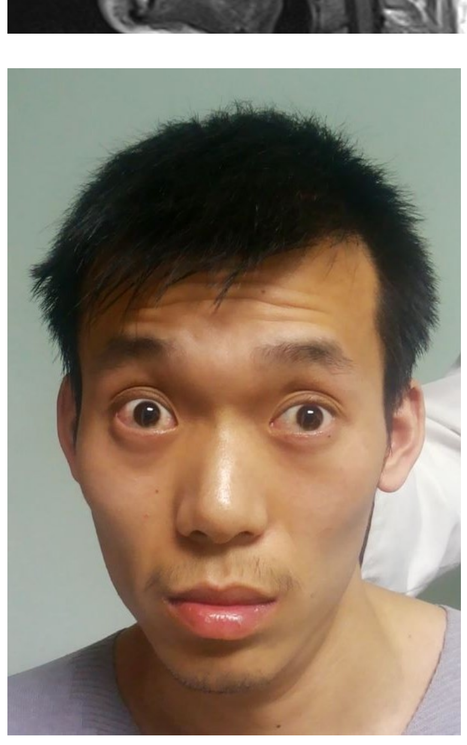
Patient 1 MRI

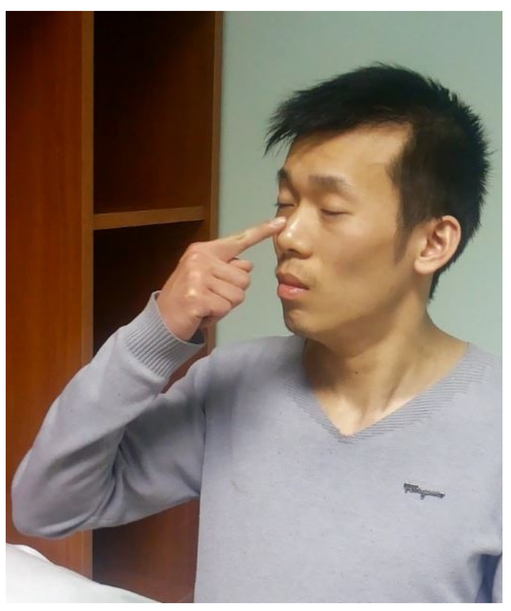


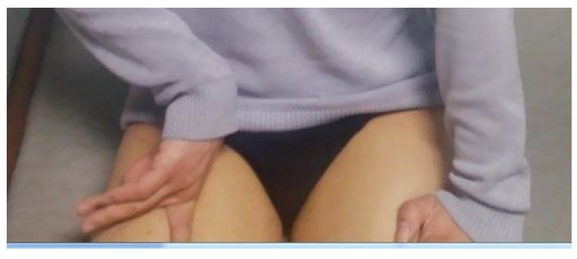


Patient 2 MRI

Patient 4







Conclusions: Past reports repeatedly claiming absence of SCA3 in Italy (1) indirectly did raise the question whether such a test is in fact warranted in our country. On the contrary, rare patients with SCA3 have already been reported in Italians (2,3). Conclusions: Our report suggests that SCA3 is indeed an infrequent but possible occurrence both in resident native and migrant population, lending support for keeping the practice of genetic

References

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