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Congenital cerebellar ataxia in a patient with SCA13: a case report

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Case report

We report the case of a 30-year-old male with **congenital cerebellar ataxia** who was referred to the neurology department of Careggi Hospital in Florence.
Since he was a child he fell often, so by the age of three he had already undergone neurological examinations in Sardinia (his home region), including a genetic test for Friedreich ataxia which was negative and a **brain MRI** that showed **cerebellar atrophy**, most marked at the level of the vermis and to a lesser extent at the cerebellar hemispheres. The patient reported that his mother also had ataxic gait.
The motor disorder remained **stable** over the years. No history of seizures was reported.
The patient also had a mood disorder classified as **bipolar disorder** and was treated with lamotrigine.
His neurological examination showed limb ataxia and an ataxic gait, cerebellar-type dysarthria, gaze-evoked nystagmus with saccadic pursuit. Deep tendon reflexes were increased in the lower limbs, muscle tone was normal. The Scale for the Assessment and Rating of Ataxia (SARA) score was 10,5. We performed Cerebellar Cognitive Affective/Schmahmann Syndrome Scale (CCAS-Scale) which resulted in 101/120 and mainly showed a **verbal fluency deficit**.
On suspicion of hereditary ataxia, we performed a genetic analysis that identified the **heterozygous p.Arg423His variant in the KCNC3 gene**, responsible for **Spinocerebellar ataxia 13** (SCA13) and typically associated with congenital disease onset.

What is SCA13?

Spinocerebellar ataxia 13 (SCA13) is a **rare autosomal-dominant cerebellar ataxia,** which is caused by a heterozygous mutation in the **KCNC3 gene**.
This gene encodes the potassium voltage-gated channel subfamily C member 3 (KCNC3), which is important for regulation of the action potential and properties of bursting neurons. There are **several pathogenic variants** that, by different mechanisms, lead to dysregulation of KCNC3.
In literature there are only a few families described worldwide affected by SCA13 and with different clinical phenotypes.
A common feature is the presence of **cerebellar atrophy** on brain MRI.
Known pathogenic variants of KCNC3 are associated with different phenotypes, although there is limited data available today to establish genotype-phenotype correlations.
Three different phenotypes are described, whose main characteristics are outlined in the table.

	Cerebellar ataxia with congenital onset	**Cerebellar ataxia with childhood onset**	**Cerebellar ataxia with adult onset**
Progression over time	Non-progressive	Slow-progression	Slow-progression
Associated clinical features	-Delayed motor milestones -Mild-to-moderate cognitive impairment Some patients may also experience: - seizures - psychiatric manifestations -hyperreflexia	-Delayed motor milestones -Moderate intellectual disability	Mild cognitive impairment
Associated mutation	p.Arg423His	p.Phe448Leu or p.Val535Met	p.Arg420His

Tab. Main characteristics of the three clinical phenotypes described for SCA13, which are associated with different mutations

Conclusions

To the best of our knowledge, this is the first description of an Italian patient affected by SCA13.
Our patient presents clinical and genetic features that are in agreement with those of similar cases described in the literature, which are however very limited.
This case report may therefore contribute to a broader collection of data on SCA13, helping to better define the phenotype associated with this mutation.

References
Waters MF, Spinocerebellar Ataxia Type 13, GeneReviews, Last Update: June 4, 2020