Expanding the *SPG11* Mutation Spectrum: A Case of Hereditary Complex Spastic Paraplegia with a Novel *SPG11* Truncating Variant and 9p24.3 Deletion

Sofia Iaselli, MD[1], Giulia Scacciatella, MD[1], Arianna Manini, MD[2], Daniela Di Bella, MD[3], Serena Leoni[4], Alessandra Sironi[4], Jacopo Spagliardi, MD[1], Valerio Patisso, MD[1], Claudia Morelli, MD[4], Alessio Maranzano, MD[4], Stefano Messina, MD[4], Federico Verde, MD[2,4], Cinzia Gellera, MD[3], Vincenzo Silani, MD[2,4], Antonia Ratti[4,5], Nicola Ticozzi, MD, phD[2,4].

1 Neurology Residency Program, Università degli Studi di Milano, Milan, Italy. 2 Department of Pathophisiology and Transplantation, "Dino Ferrari" Center, Università degli Studi di Milano, Milan, Italy. 3 Unit of Genetics of Neurodegenerative and Metabolic Diseases, Fondazione IRCCS Istituto Neurologico C. Besta, Milan, Italy. 4 Department of Neurology-Laboratory of Neuroscience, IRCCS, Istituto Auxologico Italiano, Milan, Italy. 5 Department of Medical Biotechnology and Translational Medicine, Università degli Studi di Milano, Milan, Italy.

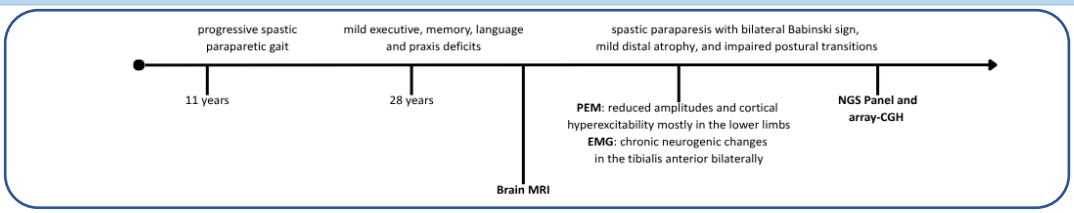
Background

Hereditary spastic paraplegias (HSPs) are a group of **rare**, clinically and genetically heterogeneous neurodegenerative disorders characterized by progressive spasticity and weakness of the lower limbs. Among autosomal recessive forms, **Hereditary spastic paraplegia type 11 (HSP11)** is one of the most frequent, caused by biallelic loss-of-function mutations in ***SPG11***, which encodes spatacsin. It is associated with **early-onset, complex phenotypes** (e.g., cognitive impairment, sphincter disturbances) and radiological hallmark features such as **thinning of the corpus callosum** (TCC) and the "**ears of the lynx**" sign.

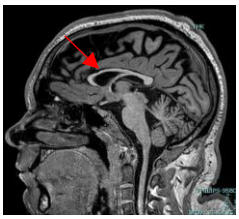
Methods

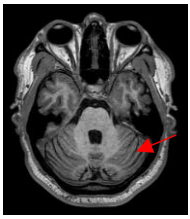
We evaluated a 28-year-old patient through neurological, neurophysiological, neuroradiological and neuropsychological assessments. **Targeted next-generation Sequencing (NGS)** of a broad panel of genes associated with inherited HSPs, as well as **array-comparative genomic hybridization (array-CGH)** were performed on the proband and the parents.

Results

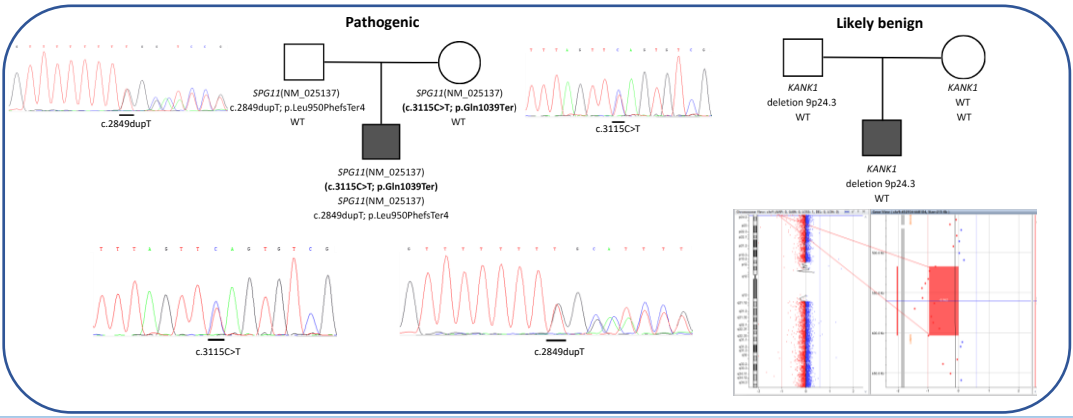


TCC in **T1**-weighted MRI, sagittal view





Cerebellar atrophy in **T1**-weighted MRI, axial view



Conclusions

- This case widens the ***SPG11*** mutational landscape by identifying a **novel truncating variant**.
- The **rare 9p24.3 deletion** involving ***KANK1*** is **likely benign** since it was detected also in the asymptomatic proband's father.
- Integrating genetic, imaging, and neurophysiological analyses is essential to decode complex HSP cases and contextualize novel variants.