Epilepsy and Movement Disorders: One Gene, Multiple Faces. A case report of PRRT2-related disorder.

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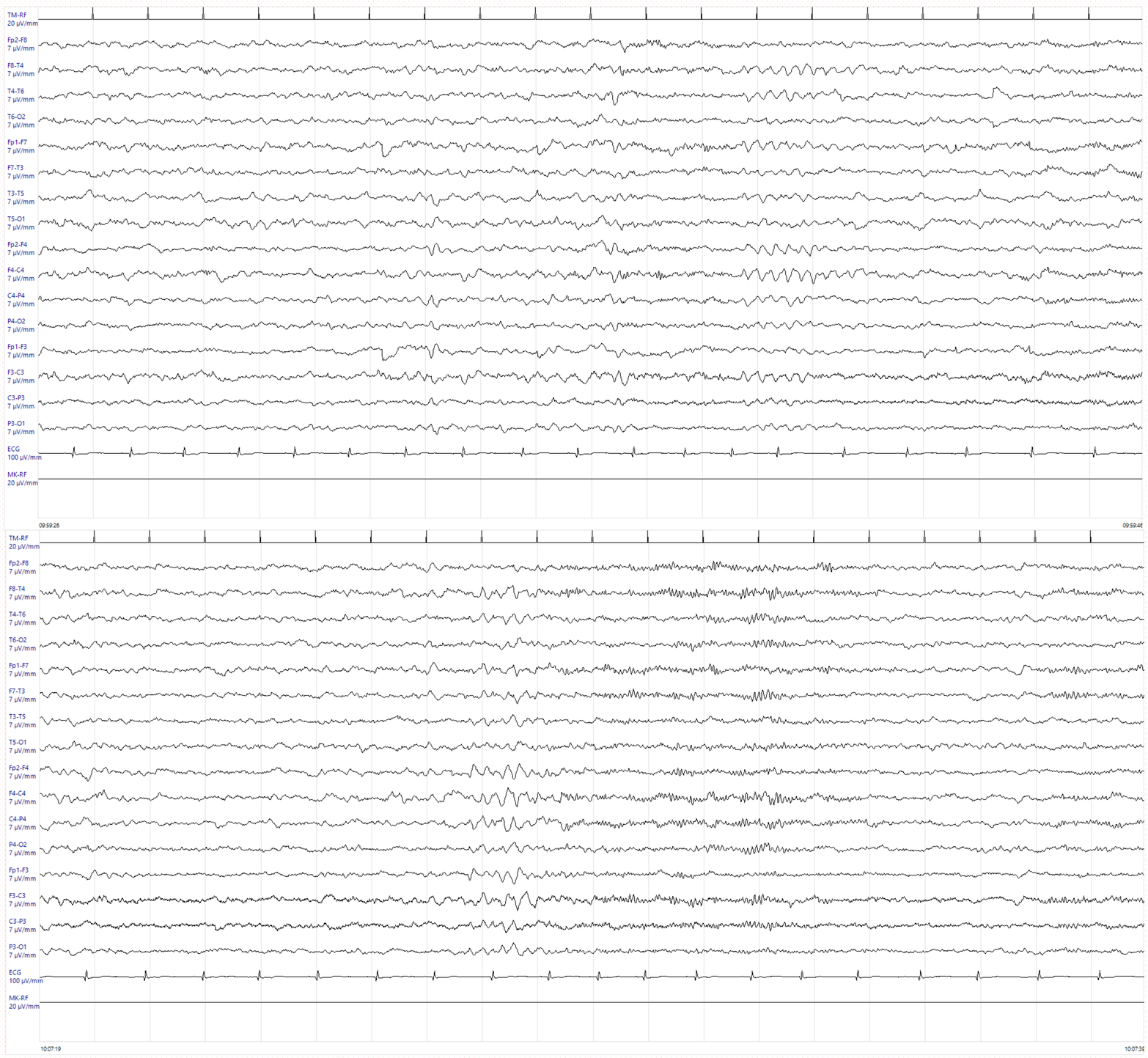
Objectives The proline-rich transmembrane protein 2 (PRRT2) is a synaptic protein involved in neurotransmitter vesicle release. PRRT2 protein is highly expressed in the cerebellum, cerebral cortex, basal ganglia, and hippocampus. Variants in PRRT2 have been identified as a cause of several neurological disorders, including epilepsy, movement disorders, and headache. Heterozygous pathogenic variants in the PRRT2 gene are associated with Infantile Convulsions with Paroxysmal Choreoathetosis, Paroxysmal Kinesigenic Dyskinesia , and Benign Familial Infantile Epilepsy, all of which follow an autosomal dominant (AD) inheritance pattern. These three nosological entities can be grouped under the umbrella term PRRT2-related disorder, which encompasses a spectrum of clinical phenotypes characterized by three main features: epilepsy, movement disorders, and migraine. In this report, we describe a case of two brothers presenting with neurological disorders PRRT2-related.

Materials We report a case of a young man of 22 years old presenting with generalized tonic-clonic seizures since the age of three years (four episodes in his life), and of his younger brother affected by paroxysmal kinesigenic dyskinesia. The genetic testing revealed the presence of the heterozygous pathogenic variant c.649dupC (single allele) in the *PRRT2* gene. Both patients presented dyslipidemia and also presented the heterozygous variant c.2043C>A in the *LDLR* gene, also identified in their older sister. Other members of the paternal family have hypercholesterolemia but the gesting testing was not yet performed.



Results Molecular analysis revealed the presence of the heterozygous pathogenic variant NM_145239.3:c.649dup, p.(Arg217Profs*8)* in the PRRT2 gene, and the heterozygous pathogenic variant NM_000527.5:c.2043C>A, p.(Cys681) in the LDLR gene. These results were consistent with the diagnosis of epilepsy and familiar hypercholesterolemia.

Brain RMI and standard EEG were negative, EEG in sleep deprivation showed paroxysmal abnormalities with diffuse expression, more prominent over the bilateral fronto-centro-temporal regions, and more evident during sleep.

Discussion The results of the molecular analysis and instrumental examinations were discussed within a multidisciplinary team. After clearly informing the patient, antiseizure treatment with Levetiracetam 500 mg twice daily was initiated, which was well tolerated and permitted the seizure freedom.

Conclusion This case report highlights the importance of considering *PRRT2*-related disorders in families presenting with early-onset epilepsy and paroxysmal movement disorders, even if the two disturbances were present by two brothers.

24-28 Ottobre 2025
Padova Congress
55° CONGRESSO SOCIETÀ ITALIANA DI NEUROLOGIA