Clinical And Genetic Spectrum of Myotonia Congenita in Turkish Children

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OBJECTIVES

Myotonia congenita (MC) is the most common form of nondystrophic myotonia and is caused by Mendelian inherited loss-of-function mutations in the *CLCN1* gene encoding the voltage-gated chloride channel of skeletal muscle. These mutations reduce the stabilizing Cl– conductance and cause episodes of muscle stiffness. More than 200 pathogenic variants (mostly missense and nonsense) have been identified. But rarely deletions and duplications have also been detected. This study aimed to describe the clinical and genetic spectrum of MC in a large pediatric cohort.

METHODS

Demographic, genetic, and clinical data of the patients younger than 18 years from 11 centers in different geographical regions of Türkiye were retrospectively investigated (Figure I).

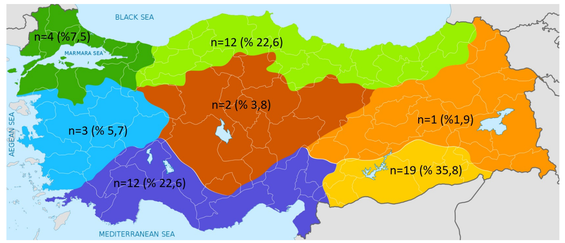

Figure I. Distribution of cases by geographical regions of Türkiye

RESULTS

Fifty-three patients (mean age:15.3 years, 75.5% males, with 86.8% Becker, 13.2% Thompsen form) from 34 families were included. Consanguineous marriage rate was 67.9%. 71.7% of patients had a family member with MC. The mean age of disease onset was 5.6 (±4.2) years. 90.6% of the patients described the warm-up phenomenon, 41.5% an increase in complaints by cold. 83% of patients had a hypertrophic appearance. 96.2% grip, 79.2% percussion-activated myotonia were observed. Only myotonia was found in 24 patients who underwent electromyography, and myotonia with myopathy in 7 patients. Overall 23 different mutations (3/23 were novel) were detected in 51 patients, and large exon deletions were identified in two siblings (Figure II). Most of the mutations were missense and nonsense variants (Figure II). Thomsen and Becker forms were concomitantly observed in one family. Carbamazepine (47.2%), mexiletine (32.1%), phenytoin (3.8%) were preferred for treatment. 66% partial, only 13.2% complete treatment response was observed.

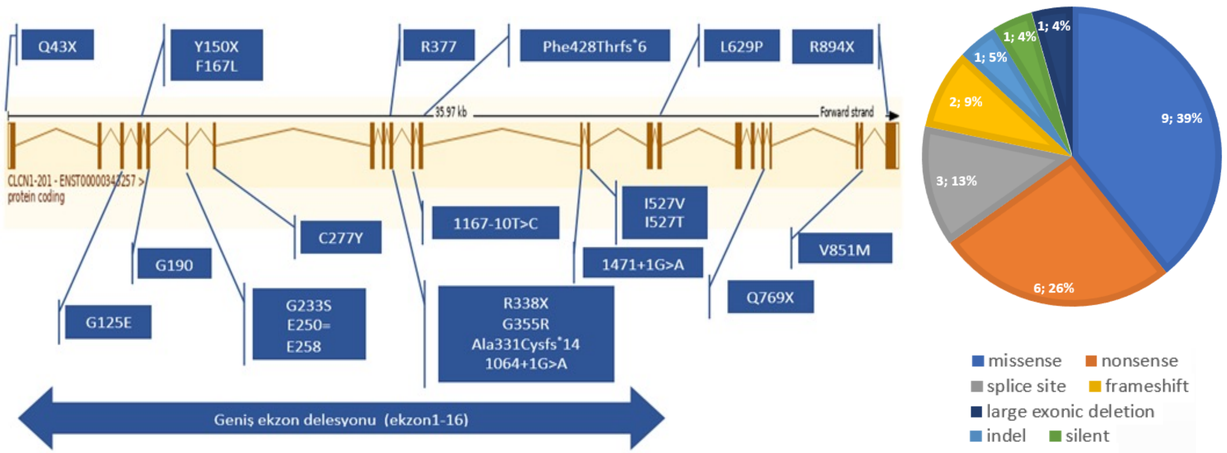

Figure II. Mutation spectrum of cases

CONCLUSION

This study is the most extended pediatric cohort of turkish individuals until now and will contribute to a better knowledge of the genotypic and phenotypic characteristics of MC patients in Türkiye. The clinical and genetic heterogeneity, as well as the limited response to current treatment options, constitutes an ongoing challenge. In our cohort, recessive MC was more frequent and novel mutations will contribute to the literature.

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