THE GENETIC HETEROGENEITY IN NEUROMUSCULAR DISORDERS: A STUDY OF NEXT-GENERATION SEQUENCING RESULTS

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Background and Aim. In the last years importance of genetic testing in diagnostics of neuromuscular disorders significantly increased. Next-generation sequencing (NGS) was introduced into the diagnostic routine of neuromuscular disorders and provided new information on the heterogeneous molecular etiology of these disorders. Our study aimed to determine the diagnostic outcome of NGS in patients with suspected genetic neuromuscular disorders.

Material and Methods. This single-center study included 23 patients with a suspected neuromuscular disorder that was not confirmed by previously performed other genetic testing methods in 2021. NGS results and clinical data were collected to investigate an underlying genetic cause and characterize the study cohort.

Results. 15 (65.2%) of the patients were adults. The patients' mean age was 31.63 years and it ranges from 2 to 75 years. The patients' mean age, when the first presentation of the symptoms was noticed, was 23.62 years and ranges from birth to 72 years. NGS revealed gene variants in 19 (82.6%) patients in total. 13 of these 23 (56.52%) patients had pathogenic or likely pathogenic gene variants, and 6 (26.08%) had a variant of uncertain significance. All patients had unique gene variants. 10 of these 19 (52.63%) patients had gene variants not mentioned in the literature. 2 of 19 (10.52%) patients had more than one gene variant possibly explaining disease phenotype. Also, NGS confirmed genetic diagnoses in 6 of 23 (26.08%) patients with no found data or normal results of electromyoneurography. Most diagnoses corresponded to muscular dystrophies/myopathies (69.23%).

Conclusions. NGS can unravel the genetic etiology in more than half of the cases. Although neuromuscular disorders present with similar phenotypes, NGS showed high genetic heterogeneity in these disorders. Knowledge of the exact molecular cause of the neuromuscular disorder is important to provide appropriate treatment and prognosis.

Keywords: heterogeneity, neuromuscular disorders, next-generation sequencing