論 文 要 旨

Genetic profile and onset features of 1005 patients with Charcot-Marie-Tooth disease in Japan

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Objective To identify the genetic characteristics in a large-scale of patients with Charcot-Marie-Tooth disease (CMT).

Methods From May 2012 to August 2016, we collected 1005 cases with suspected CMT throughout Japan, whereas *PMP22* duplication/deletion were excluded in advance for demyelinating CMT cases. We performed next-generation sequencing targeting CMT-related gene panels using Illumina MiSeq or Ion Proton, then analysed the gene-specific onset age of the identified cases and geographical differences in terms of their genetic spectrum.

Results From 40 genes, we identified pathogenic or likely pathogenic variants in 301 cases (30.0%). The most common causative genes were *GJB1* (n=66, 21.9%), *MFN2* (n=66, 21.9%) and *MPZ* (n=51, 16.9%). In demyelinating CMT, variants were detected in 45.7% cases, and the most common reasons were *GJB1* (40.3%), *MPZ* (27.1%), *PMP22* point mutations (6.2%) and *NEFL* (4.7%). Axonal CMT yielded a relatively lower detection rate (22.9%), and the leading causes, occupying 72.4%, were *MFN2* (37.2%), *MPZ* (9.0%), *HSPB1* (8.3%), *GJB1* (7.7%), *GDAP1* (5.1%) and *MME* (5.1%). First decade of life was found as the most common disease onset period, and early-onset CMT cases were most likely to receive a molecular diagnosis. Geographical distribution analysis indicated distinctive genetic spectrums in different regions of Japan.

Conclusions Our results updated the genetic profile within a large-scale of Japanese CMT cases. Subsequent analyses regarding onset age and geographical distribution advanced our understanding of CMT, which would be beneficial for clinicians.