Charcot-Marie-Tooth disease: frequency of genetic subtypes in Sardinian population

Lorefice L.,[1] Murru M.R.,[1] Coghe G., [1] Corongiu D., [1] Tranquilli S.,[1] Fenu F,[1] Frau J.,[1] Mamusa E.,[1] Vannelli A.,[2] Tacconi P.,[3] Marrosu G.,[2] Cocco E.,[1] Marrosu M.G.[1]

[1] Multiple Sclerosis Centre, ASL8- Binaghi Hospital, University of Cagliari, Italy
[2] Neuromuscular Centre, Binaghi Hospital, ASL8- Cagliari, Italy
[3] Institute of Neurology, AOU Cagliari, Italy

Background. Charcot-Marie-Tooth (CMT) disease is a hereditary sensory motor neuropathy characterized by great heterogeneity in clinical features and inheritance. Currently, more than 40 genes and loci are known for being involved in the diseases' pathogenesis, showing great variability of genetic subtypes in different geographical area.[1]

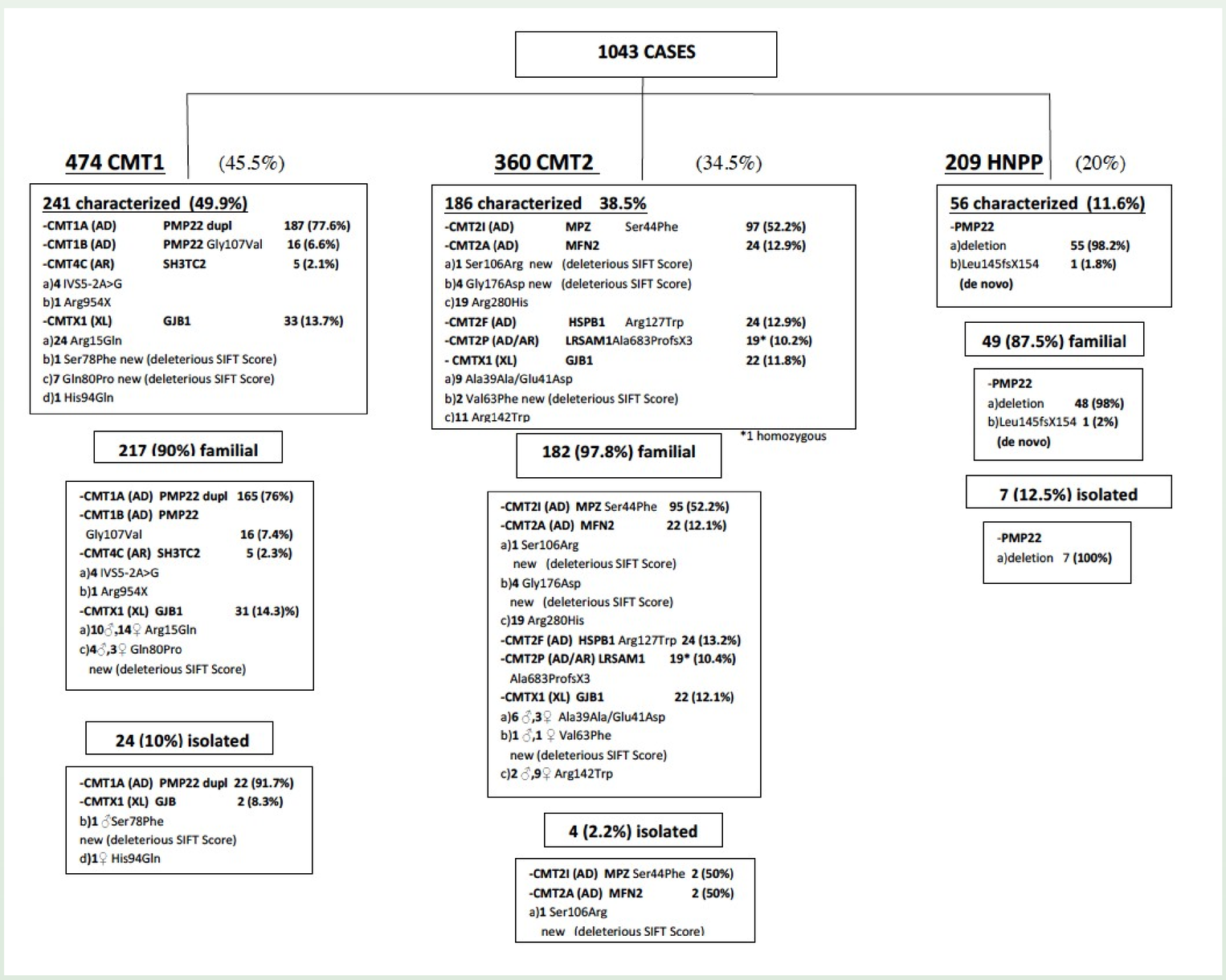
Aims. The objective of this study is to assess genetic subtypes of CMT disease in Sardinia, an island characterized by homogeneous and peculiar genetic background, comparing them with others from regions of the Mediterranean area.

Methods.

A genetic screening was performed for index cases (CMT1, CMT2, and hereditary neuropathy with susceptibility to pressure palsies [HNPP]). The type and frequency of mutations for each CMT group were also reported, specifying both familial and isolated cases.

RESULTS

A total of 1,043 patients were evaluated. Molecular diagnosis was achieved in 483 (46.3%) cases: 241 (49.9%) CMT1, 186 (38.5%) CMT2 and 56 (11.6%) HNPP patients. In CMT1 cases, PMP22 gene duplication was the most frequent genetic diagnosis (187; 77.6%), followed by mutations in the GJB1 gene (33; 13.7%) and PMP22 Gly107Val point mutation (16; 6.6%). The CMT2 group comprised 97 (52.2%) patients carrying a mutation in the MPZ gene (Ser44Phe), 24 (12.9%) in MFN2 and HSPB1, 22 (11.8%) in GJB1, and 19 (10.2%) in LRSAM1. In the HNPP group, the majority of patients reported PMP22 gene deletion (55; 98.2%). Five novel mutations were detected: 2 in CMT1 and 3 in CMT2.



Discussion and Conclusions. The frequency of genetic subtypes in Sardinian CMT cases showed several differences compared to others from adjacent regions.[2,3] Additional studies are needed to better know the CMT genetic distribution in the Mediterranean area.

References

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