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Distribution of limb girdle muscular dystrophy subtypes among Portuguese patients

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Introduction:

Although the limb girdle muscular dystrophies (LGMD) are collectively characterized by progressive muscle weakness, they exhibit wide clinical and genetic heterogeneity. Over 23 *loci* have been identified; eight are autosomal dominant subtypes (LGMD1A-1H) and fifteen are autosomal recessive (LGMD2A-2O). The prevalence and relative distribution of the different subtypes varies widely between populations. Here we present an overview of the LGMD profile in our population, as ascertained in patients referred from all over the Country over a period of 15 years, with clinical phenotypes ranging from severe childhood-onset LGMD, adult-onset LGMD and distoproximal myopathy, to barely symptomatic presenting only hyperCKemia.

Methods:

Inclusion criteria were essentially compatible clinical presentation and/or muscle biopsy (histology and immunocytochemistry). A total of 425 families were selected, representing 525 genetic tests for different genes: *CAPN3 (n=87)*, *DYSF (n=105)*, *SGCG (n=94)*, *SGCA (n=46)*, *SGCB (n=39)*, *SGCD (n=18)*, *TCAP (n=6)*, *FKRP (n=55)*, *TTN (n=4)*, *ANO5 (n=11), MYOT (n=5)*, *LMNA (n=46)*, and *CAV3 (n=9)*.

Results:

Differential diagnosis was achieved in 183 unrelated families, where a total of 92 different mutations were identified, 44 of which were novel. The gamma-sarcoglycanopathies were the most frequent subtype (13.4%), clearly as a result of a founder effect among families of gypsy (Roma) ethnicity and the presence of a frequent mutation thought to be of North African origin. This was followed by the dysferlinopathies (10.4%), with no particular hotspot along the 56 exons, except for two private mutations. All other forms detected each represented under 5% of the cases, and 56.9% remained genetically unresolved.

Conclusion:

The profile of our patients differs slightly from that of other large cohorts in studies reported for the European, North American, Australian and Brazilian populations. In this group of disorders with wide genetic heterogeneity, knowledge of the subtype and mutational spectrum in our population facilitates the diagnostic approach.