Genetic landscape of Congenital Muscular Dystrophy(CMDs) from central Aegean part of Turkey

Didem Soydemir[1], Berk Ozyılmaz[2], Ipek Polat[1], Pinar Edem[3], Gamze Sarıkaya Uzan[1]
Figen Baydan[4], Semra Hiz[1 5], Sebahattin Cirak[6], Uluc Yis[1]

[1] Dokuz Eylul University Faculty of Medicine, Department of Pediatrics, Division of Pediatric Neurology, Izmir, Turkey
[2] University of Health Sciences, Tepecik Training and Research Hospital, Genetic Disease Center, Izmir, Turkey
[3] Bakircay University Cigli Training and Research Hospital , Department of Pediatrics, Division of Pediatric Neurology, Izmir, Turkey,
[4] University of Health Sciences, Tepecik Training and Research Hospital, Department of Pediatrics, Division of Pediatric Neurology, Izmir, Turkey,
[5] Izmir Biomedicine and Genome Center, Dokuz Eylul University Health Campus, Izmir, Turkey
[6] University of Cologne Faculty of Medicine and University Hospital, Department of Pediatrics, Center for Molecular Medicine (CMMC), Cologne, Germany

ICNC 2022 — 17th INTERNATIONAL CHILD NEUROLOGY CONGRESS — ANTALYA, TURKEY I OCTOBER 3-7, 2022

Objectives

- Congenital muscular dystrophy is a group of genetically heterogenous neuromuscular disorders involving distinct core phenotypes with variable prognosis.[1]
- Main clinical manifestations are early onset hypotonia and delay/arrest of gross motor functions with hyperCKemia and dystrophic muscle pathology.
- Overlap situations and geographic differences exist in the nature of the disease.[2,3]
- The main goal of our study is to identify the genotype-phenotype spectrum of CMDs in central Aegean part of Turkey.

Materials and Methods

01 Assesment of all patients underwent further investigation for Congenital Muscular Dystrophy

02 Retrospective evaluation of subjects registered from 2010 to 2020 to our department

03 Data collection(clinical,laboratory,histopathology genetic) from electronic medical records

04 Analysis and summary of descriptive statistics regarding recent classifications*

Figure-1: Methodology of our retrospective study

*All patients in 3 categories:
(a) definite core phenotypes with genetic analysis
(b) probable core phenotypes with evidence of hyperCKemia and/or dystrophic patern on muscle biopsy
(c) unclassified other CMDs.

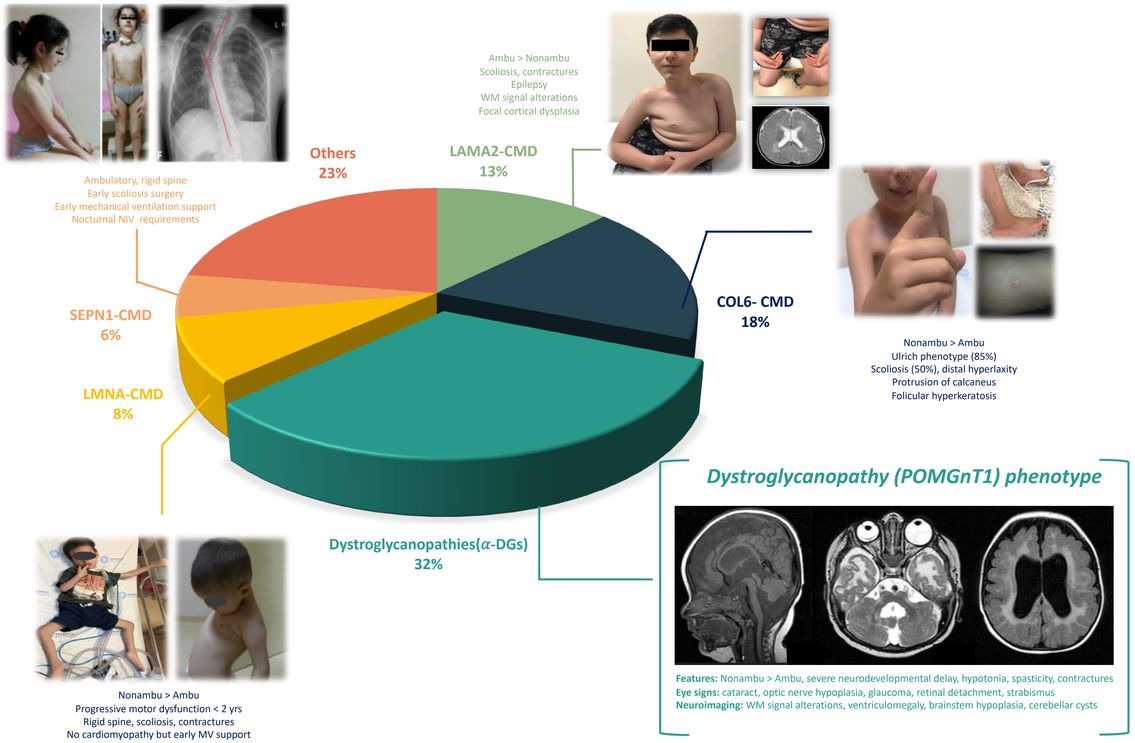

Figure-2: Summary of results with core phenotypes and clinical features of POMGnT1 patients

Conclusion

In contrast to population based studies in Europe;

- **Alfa-dystroglycanopathies(α-DGs)** were the most common phenotype in Turkey. ***POMGnT1*** was the most common identified gene.
- ***c.1814 G>A variant*** in POMGnT1 was fairly frequent in Turkish population suggesting a ***founder effect.***

Results

- We identified 71 subjects (37 male, 34 female) from 62 unrelated families.
- Definite diagnosis(distinct core phenotype plus genetic analysis) and consanguinity rate were 73 %(n=52) and 61 %(n=34) respectively.
- Common initial symptom was early onset muscle weakness with hypotonia.
- The most common phenotype was **alfa-dystroglycanopathies**(n=23) followed by **COL6** (n=13) and **LAMA-2** (n=9) related myopathies.
- Other CMD spectrum genes were *LMNA*, *SEPN1, CHKB, SYNE1* and *INPPK5.* ***(Figure-2)***
- Among dystroglycanopathies in our cohort, main clinical manifestation was in consistent with **Muscle-Eye-Brain/Fukuyama (MEB/FCMD)** disease(n=15) followed by Walker Warburg syndrome(WWS/n=4).
- Patients with ***POMGnT1*** mutations had hypotonia at birth.
- In evaluation of neuroimaging for all phenotypes, periventricular white matter changes were seen in both ***POMGnT1*** and ***LAMA-2*** mutations as major abnormality. Among all patients, ventriculomegaly and cortical dysplasia were diagnostical hallmarks respectively for these genes.

References

1.Bönnemann CG, Wang CH, Quijano-Roy S et al. Diagnostical approach to the congenital muscular dystrophies.Neuromuscular disorders,2014,24(4),289-311.
2. Zambon AA, Muntoni F. Congenital muscular dystrophies: What is new?. Neuromuscular Disorders, 2021, 31.10: 931-942.
3. Sframeli M, Sarkozy A, Bertoli M et al. Congenital muscular dystrophies in the UK population: Clinical and molecular spectrum of a large cohort diagnosed over a 12-year period. Neuromuscular Disorders,2021,27(9):793-803.
4. Ge L, Zhang C, Wang Z et al. Congenital muscular dystrophies in China. Clinical Genetics,2019,96(3), 207-215.

All authors declare no conflict of interests.
Special thanks to the parents of our cases for the display of images

didem.soydemir@deu.edu.tr