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Cardiogenetic Approach in Children Cardiomyopathies. Does It Make Change in Clinical Pathway? Results on The Basis of a Cohort of 250 Children.

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Introduction: cardiomyopathies (CMP) are highly heterogeneous in origin. Multiple phenocopies are identified on adult cohorts but less is known in children in whom CMP is a rare disease. Early 90s reports describe 20% familial origin while late international reports identify up to 50% of familial cases. Origin varies from genetic to non-genetic background. Again the variability is very high in genetic causes including sarcomeric, desmosomal, nuclear, mitochondrial and malformative origins. Different cytogenetic and molecular genetic methods were applied to reach highest detection rate of pathogenic variants. Most of rare PHENOCOPIES in CMP remain undiagnosed, lately diagnosed or misdiagnosed.

Methods: a multidisciplinary transversal and longitudinal approach is applied in this cohort of 252 patients affected by CMP. A multi-organ approach including the investigation of metabolic, hormonal, and genetic factors. The algorithm is not based on the exclusion but the integration of different factors. In other words, we believed in the multifactorial and multigenic model of CMP rather than unifactorial origin of the disease.

Results: we identified 56% familial background. The majority of genetically positive patients carried sarcomeric mutations. RASopathies represented the majority of early onset HCMP. Rare DCMP phenocopies were recognized: Barth Syndrome (3 families), TMEM70 (2 families), Laminopathies (4 families), EDS (1 family), desmosomal (10 families), desminopathies (1 family), and filaminopathy C (3 families). A comprehensive illustration of the cardiogenetic pathway will be explained. We shall illustrate the systematic “red flag” approach performed in the diagnosis of children CMP.

Conclusions: This cohort represents a preliminary example of personalized medicine approach in children cardiogenetics and how identifying underlying diagnosis can change the clinical course and sometimes the therapeutic approach for the individual and families of children affected by CMP. To the best of our knowledge this approach helps in ameliorating the clinical approach and outcome in rare forms of children CMP.

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