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Diagnostic approach of hereditary red blood cell membranopathies: From Osmotic Gradient Ektacytometry (OGE) to Next Generation Sequencing (NGS)

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Introduction

Hereditary red blood cell (RBC) membranopathies are characterized by mutations in genes encoding skeletal proteins that alter the membrane complex structure. Hereditary spherocytosis (HS) is the most common inherited RBC membranopathy leading to hereditary hemolytic anemia with a worldwide distribution and an estimated prevalence, in Europe, of about 1:2000 individuals. The recent availability of targeted next generation sequencing (t-NGS) and its combination with RBC deformability measured with a laser-assisted optical rotational ektacytometer (LoRRca) has demonstrated to be the most powerful contribution to lower the percentage of hereditary hemolytic anemia undiagnosed cases. In order to know the kind and frequency of RBC membrane mutations in our geographical area (Catalonia) and to better understand their pathophysiology, 42 unrelated, non-transfusion-dependent (NTD) patients with hereditary hemolytic anemia have been studied by combining t-NGS and LoRRca. The osmoscan module of LoRRca provides three rheological profiles that reflect the maximal deformability (EImax), osmotic fragility (Omin), and hydration state (Ohyper) of RBCs and contribute to a better understanding of the contribution RBC rheology to the severity of anemia. From the 42 patients studied, 37 were

suspected to be a RBC membrane defect due to phenotypic characteristics and abnormal RBC morphology and, from these, in 31 patients (83.8%of cases) the mutation was identified by t-NGS. No definite diagnosis was achieved in 11 patients (26.2% of cases), including 6 out of 37 cases, with suspected membranopathy, and 5 with unclassifiable HHA. In all these undiagnosed patients, the existence of hemoglobinopathy and/or enzymopathy was ruled out by conventional methods

Image

Recent Publications

1. Requena-Méndez, A., Bisoffi, Z., Vives-Corrons, J.-L., Gascon, J, ., Plasència (2020). A European expert network on rare communicable diseases and other rare diseases linked to mobility and globalisation focused on health care provision (EURaDMoG): a feasibility study. Orphanet Journal of Rare Diseases, 15 (1), art. no. 291

2. Krishnevskaya, E., Rizzuto, V., Payán-Pernía, S., Remacha, Á., Torrent, M, Ruiz, A., Badell, I., Vives- Corrons, J.-L (2020). Coinheritance of hereditary ellyptocytosis, pyruvate kinase, and glucose-6-phosphate dehidrogenase mutations. A rare anemia diagnostic paradigm. International Journal of Laboratory Hematology, 42 (2), pp. e55-e58

3. Vives Corrons, J.-L., De Sanctis, V Rare anaemias, sickle-cell disease and covid-19. (2020) Acta Biomedica, 91 (2), pp. 216-217.

4. Vives-Corrons, J.-L., Krishnevskaya, E., Rodriguez, I.H., Ancochea, A.
(2020). Characterization of hereditary red blood cell membranopathies using combined targeted next-generation sequencing and osmotic gradient ektacytometry. International Journal of Hematology. https://doi.org/10.1007/s12185-020-03010-9

5. Krishnevskaya, E., Payán-Pernía, S., Hernández-Rodríguez, I., Remacha Sevilla, Á.F., Ancochea Serra, Á., Morales-Indiano, C., Serra Ferrer, M., Vives-Corrons, J.-L (2020). Distinguishing iron deficiency from beta-thalassemia trait by new generation ektacytometry. International Journal of Laboratory Hematology. doi: 10.1111/ijlh.13362

Keywords: Hemoglobinopathy, Hereditary spherocytosis, ektacytometer

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