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ON THE IMPORTANCE OF GENOTYPE AND PHENOTYPE

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EDITORIAL

Genetic disorders are often misunderstood, poorly studied, and inadequately addressed by health professionals. This is apparently a matter of frequency, as this type of disorder is reported in 5 cases per 10 000 live births (7% of the world population), being the cause of 80% of the so-called rare diseases (1).

Some genetic diseases are well known, such as Down syndrome, Duchenne muscular dystrophy, sickle cell anemia, Huntington's disease, cystic fibrosis, among others, and they are part of our daily practice as physicians, as well as part of the popular knowledge. There are also cases in which there are clinical findings consistent with these types of diseases but, in spite of this, we cannot classify them into a single syndrome.

Databases are very effective in the study of this type of cases. For example, in 1960, Dr. Victor Almon Mckusick initiated the publication of a catalog intended to document information about recognized inherited disorders, which led to the development of the Mendelian Inheritance in Man. This catalog is currently known as Online Mendelian Inheritance in Man (OMIM), and its first online version was developed in 1985. Since 1995, the OMIM has made available a free version that is edited and updated annually by the McKusick/Nathans Institute of Genetic Medicine (2).

At present, the database contains information on the relationship between genotype and phenotype for several diseases, with more than 27 000 entries including gene description, combined gene and phenotype description, phenotypic description with known molecular basis, some phenotypes with suspected Mendelian basis, as well as autosomal, mitochondrial and X- or Y-chromosome-linked diseases (2). This database, and others like it, allows clinicians to obtain data on patients with simultaneous findings in different systems of their body in which a Mendelian origin is suspected.

This issue of Case Reports presents a very interesting and rare case of a newborn with agenesis of corpus callosum, cardiac, ocular, and genital syndrome (ACOGS), which is caused by a heterozygous mutation in the *CDH2* gene on chromosome 18q12. It was first described in 2019 by Accogli *et al.* (3), who presented a study of 9 cases (out of 13 published to date) and was introduced to OMIM on June 26, 2020. ACOGS in this database is numbered 618929 for the phenotype and 114020 for the locus.

In addition to the significance of this case due to its unusual occurrence, it is essential to highlight the careful approach to the diagnosis taken by the treating team. They suspected a syndrome of Mendelian origin from a scattered and rare phenotype and, after conducting a thorough search of the available literature (and this database), it was possible to confirm that the patient had that disorder.

Cystic fibrosis is another great example of a genetic disorder with many phenotypes for consideration, presenting with pulmonary and pancreatic symptoms,

sweating disorders, and alterations in chromosomal location 7q31, 16p12 or 19q13, which demonstrates how several genes can affect the expression of a first affected gene. This can be observed in children affected by this disease, in whom early diagnoses can be made, as well as in adults in whom the diagnosis is made late because they have a much less severe variant of the disorder.

Clinicians of all specialties have the permanent and complex challenge of considering that many alterations in different systems can be regarded as part of a syndrome of genetic origin. Therefore, including the patient's perspective in the comprehensive genetic assessment is of utmost importance, whether it is to make a proper diagnosis, provide prenatal counseling, detect a disease before symptom onset, or establish the best treatment as required.

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