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STRUCTURAL CHROMOSOMAL VARIATIONS: LITERATURE REVIEW FROM A CLINICAL CASE

Vinícius Silva Garcia
Universidade Federal do Rio Grande
Rio Grande – Rio Grande do Sul
http://lattes.cnpq.br/1160725165778943

Simone Heckler de Lima
Universidade Federal do Rio Grande
Rio Grande – Rio Grande do Sul
http://lattes.cnpq.br/6970758091061715

Vitor Antônio Batista Bom Fim
Universidade Federal do Rio Grande
Rio Grande – Rio Grande do Sul
http://lattes.cnpq.br/7974732011436879

Hellen Cristina de Azevedo
Universidade Federal do Rio Grande
Rio Grande – Rio Grande do Sul
http://lattes.cnpq.br/3018460254163737

Simone de Menezes Karam
Universidade Federal do Rio Grande
Rio Grande – Rio Grande do Sul
http://lattes.cnpq.br/9162310534609511

Abstract: Structural Chromosomal Variations affect chromosomes and have the potential to cause phenotypic changes and lead to the manifestation of diseases by different mechanisms. Data found in the literature were correlated with the clinical case of a female newborn who expressed ocular and nipple hypertelorism, bilateral cleft lip, microtia, auditory canal atresia and deletions in chromosome 7 in regions q32q36 on the karyotype exam. Deletions are the main cause of genetic diseases and explain the physical alterations found while de novo mutations, as seen in this case, are more frequently associated with pathologies and are capable of affecting child development. The suspicion of a genetic cause made it possible to identify the chromosomal deletion, genetic counseling and planning a future pregnancy. Despite constant advances in the genetic area, further studies are needed.
Keywords: Genome Structural Variation; DNA Copy Number Variation; Chromosomal Aberrations; Human Genome.

INTRODUCTION

Structural Chromosomal Variation is the term used to describe quantitative and structural rearrangements that affect chromosomes and that originate from mechanisms of DNA recombination, replication and repair processes (WEISCHENDFELDT et al., 2013; SPIELMANN et al., 2018). It can be balanced, when there is no gain or loss of genetic material, as in inversions and translocations, or unbalanced, as in deletions, duplications and insertions (SPIELMANN et al., 2018). These changes can alter gene dosage, protein expression and expose inactive genes, potentially leading to phenotypic changes and diseases (WEISCHENDFELDT et al., 2013; SPIELMANN et al., 2018). It is estimated that 0.13% of individuals carry a structural alteration that manifests important clinical findings (COLLINS et al., 2020). Seen that, the objective of this work is based on the analysis of a clinical case of a newborn with structural variations and phenotypic alterations. The importance of this investigation resides in the clinical relevance of the manifestations and in their diversity of presentations, which makes it difficult to identify and interpret the expressions.

METHODOLOGY

A search was carried out in the PubMed database with terms selected according to the Medical SubjectHeading (MeSH) and the Health Sciences Descriptors system (DeCS). The keywords used in the search were "genomicstructuralvariation" OR "structuralvariation". As inclusion and exclusion criteria, the descriptors must be contained in the title or abstract fields and the studies must have been published in the last ten years. In addition, only works related to the human species were analyzed. The search was carried out in June 2021 and 730 publications were found, of which 55 were selected for reading the abstract based on the title and of these, 32 for reading in full. At the end of the process, 8 articles remained that were used to compose the literature review.

CLINICAL CASE DESCRIPTION

Full-term newborns, females, with a history of morphological ultrasound examinations performed during pregnancy suggestive of changes such as cleft lip, as well as the presence of other phenotypic changes detected postpartum, are referred to the genetics clinic. There was no history of family-inherited diseases. On physical examination, the newborn was in good general condition and had multiple morphological alterations, such as ocular and nipple hypertelorism, bilateral cleft lip, cleft palate, grade II bilateral microtia associated with bilateral atresia of

the auditory canals, the latter observed in an examination of image. After carrying out a karyotype exam, the presence of deletions in the long arm of chromosome 7 in regions q32q36 was verified.

DISCUSSION

The newborn presents phenotypic expressions explained by the deletion found in the karyotype. According to database analyses, 80% of genetic diseases are caused by deletions, while duplications lead to less severe alterations (FIRTH et al., 2009). In addition, de novo structural variations are more frequently associated with pathologies (COOPER et al., 2011). As a prototype of disease caused by deletion, Williams Syndrome can be mentioned, characterized by facial dysmorphisms, aortic stenosis, intellectual disability and specific neurobehavioral characteristics (ZHANG et al., 2013). Furthermore, population studies have found an association between structural variations and pathologies such as Autism Spectrum Disorder (ASD) (SEBAT et al., 2007)

Clinically, the phenotypic findings of the newborn are of clinical relevance, even more so if identified early, as the development of a child is shaped by the action of genetic and environmental forces (ZHANG et al., 2013). Although the karyotype exam was used for diagnosis, because it is more accessible, there are other tools such as Array-CGH and new methods that make up the Next-Generation Sequencing (NGS) and that allow more accurate detection and mapping using techniques of Whole-GenomeSequencing (WGS) (YANG, 2020).

FINAL CONSIDERATIONS

The clinical case corroborates with what is proposed by the literature about phenotypic manifestations caused by Structural Chromosomal Variations. The suspicion that these characteristics were associated with a genetic cause led to referral to the genetics outpatient clinic, which identified the deletion. Genetic counseling allowed further investigations, as well as predictions and guidance to the family regarding findings and therapeutic possibilities, since the alterations found have a negative impact on neuropsychomotor development, as well as planning for a new pregnancy. Despite the emergence of new diagnostic techniques and the creation of genetic databases, there are still many gaps in relation to the subject, of great clinical relevance, so that further studies are necessary.

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