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How might a balanced chromosomal translocation lead to a spectrum of intellectual disabilities in newborns?

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Background: Intellectual disability (ID) consists of a broad range of disorders characterized by low general intellectual functioning (IQ below 70). ID etiologic causes are heterogeneous, ranging from environmental to chromosomal and monogenic conditions. Although many autosomal genes responsible for ID are expected, only a small number of these have been identified, and up to now most progress has been made in X-linked translocation ID area; but many autosomal genes play a crucial role in the development of a central nervous system. Any change which leads to lose or reduce the function or changes the expression of them; high or low, even have a damaging effect on the functional protein might lead to different phenotypes like developmental delay, growth retardation, or intellectual disabilities.

Result & conclusion: In this paper, we discuss the importance of balanced chromosomal translocations in the cause of newborn intellectual disabilities. Balanced translocation is the result of breaking off two chromosomes and reattaching in a way that the sections of two chromosomes have switched places. These rearrangements are found as de novo events in 1/2000 live births and give rise to some congenital anomalies which are the product of submicroscopic deletions, duplications, inversion or disruption, activation, or inactivation of a gene or different genes located at or near the breakpoints in the basepair level. These apparently balanced translocations due to positional effect lead to abnormal phenotype.

Conclusion: Cryptic genomic imbalances which cause mentality are very rare conditions but new technologies like NGS long-read genome sequencing could detect breakpoint effects on live birth health and discover a new way for prenatal diagnosis.

Cancer Study

Introduction

Definition and Classification of intellectual disability:

The term Intellectual Disability (ID) was given to mental deficiency in the first edition of the Diagnostic and Statistical Manual (DSM-I; American Psychiatric Association 1952) (Sismani C, et al., 2008) and was used to classify individuals who presented with "a deficit of intelligence existing since birth, without proven brain disease or identified prenatal cause. DSM-II divided it

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based on Severity Levels into 5 sections; including borderline, mild, moderate, severe, and profound mental retardation (Matson JL, et al., 2019). IQ across the population is normally distributed with the mean set at 100 and the manifestation of ID widely differs between individuals in relation to the degree of impairment however low general intellectual functioning or Intelligence Quotient (IQ) less than 70 is defined as ID (Moysés-Oliveira M, et al., 2015). Severe ID is generally diagnosed with an IQ below 50 and substantial limits in activities of daily life, it should be noticed that IQ tests are not always applicable because of young age (e.g., children below 3 years) or associated sensory-motor issues and gross under stimulation (De Ligt J et al., 2012). IDs have a variety of causes and many of them are not known but mainly divided into genetic abnormalities including chromosomal or monogenic conditions and environmental exposure (Lee K et al., 2023).

Genetic diagnosis of ID:

Genetic diagnosis is essential not only for accurate genetic counseling of recurrence risks and prenatal diagnosis but also for the appropriate management and almost 15% to 40% of ID is due to genetic factors (Hao D et al., 2021). It is estimated that more than 1,000 different genes mutation, and rare de novo point mutations could be the main cause of ID (Karam SM et al., 2015, Jacquemont S et al., 2014, Segawa M, 2005).

Balanced Chromosomal rearrangement via abnormal phenotype:

Reciprocal translocations are a transfer of genetic material between chromosomes and this exchanged is with no apparent loss. The carriers are usually phenotypically normal but about 0.2% of their newborns have structural chromosome abnormality due to mispairing of translocated chromosomes and transmission of chromosomal abnormalities from affected parents, although in about 6% of de novo cases, an abnormal phenotype is present (Bennett P et al, 2010, Zhang K et al., 2018, Zhang HG et al, 2016). Scientist believes that the risk of phenotypic abnormalities is different (Warburton D, 1991). Some of these balanced rearrangements may disrupt candidate genes or the formation of chimer genes, or change the expression of genes near the breakpoint via the positional effect which may lead to clinical phenotypes (Liao H-M et al., 2011, Leegte B et al., 1998).

Mapping the Balanced Chromosomal Translocation:

The effect of these balances couldn't diagnose by chromosome banding studies, although standard high-resolution karyotype analysis is the first step to find the imbalance rearrangements but high-resolution techniques need to visit the influence of rearrangements at base pair level such as FISH or NGS (Gribble Set al., 2005, Kalscheuer VM et al., 2009). Sometimes translocation breakpoints may alter the expression of some genes and RNA sequencing is an effective methodology for precise detection (Aristidou C et al., 2017).

Conclusion:

Autosomal gene mutations and chromosomal rearrangements have a principal role in the etiology of ID and small subtelomeric deletions have been found in up to 7% of ID patients (Ropers HH et al., 2005 19) but cryptic genomic imbalances due to balanced chromosomal translocations cause of mentality are very rare condition. However genetic counseling, Prenatal diagnosis tests, or, preimplantation genetic diagnosis (PGD) for balanced translocation carriers are recommended as to increased risk of implantation failure, pregnancy loss, or abnormal offspring.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethics approval

Not applicable