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Inherited microdeletion of the short arm of chromosome 13 in a twin pregnancy (46, XX) and (92, XXXX)

Microdeleción heredada del brazo corto del cromosoma 13 en un embarazo gemelar (46, XX) y (92, XXXX)

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Abstract

Chromosome 13 is one of the five acrocentric chromosomes. The heteromorphism of acrocentric chromosomes corresponds to structural variations without phenotypic consequences that occur randomly, with deletion heteromorphism being rare, especially with a hereditary pattern. This study describes a microdeletion in the short arm of chromosome 13 identified in a 37-year-old pregnant woman with a history of recurrent pregnancy loss and in her twin fetuses. A cytogenetic analysis was performed through fetal karyotyping from chorionic villus sampling, revealing the same chromosomal deletion in both fetuses, which was also present in the mother. The father's analysis showed a normal karyotype, suggesting a maternal origin of the alteration. Although these types of deletions are usually clinically insignificant, their association with reproductive issues is not yet fully understood. This case highlights the importance of cytogenetic studies in women with a history of recurrent pregnancy loss and the need for further research to determine the impact of these structural alterations on pregnancy viability and genetic counseling.

KEY WORDS

Chromosome 13, Deletion, Chromosomal disorder, Recurrent pregnancy loss.

Resumen

El cromosoma 13 es uno de los cinco cromosomas acrocéntricos. El heteromorfismo de los cromosomas acrocéntricos corresponde a variaciones estructurales sin consecuencias fenotípicas que ocurren de forma aleatoria, siendo raros los casos de heteromorfismo por deleción, especialmente con un patrón heredado. En este estudio, se describe una microdeleción en el brazo corto del cromosoma 13 identificada en una gestante de 37 años con antecedentes de pérdidas gestacionales recurrentes y en sus fetos gemelares. Se realizó un análisis citogenético mediante cariotipo fetal a partir de biopsia de vellosidades coriónicas, encontrando en ambos la misma deleción cromosómica presente en la madre. El análisis del padre mostró un cariotipo normal, lo que sugiere un origen materno de la alteración. Aunque este tipo de deleciones suelen carecer de relevancia clínica, su asociación con problemas reproductivos aún no está completamente comprendida. Este caso subraya la importancia de los estudios citogenéticos en mujeres con antecedentes de pérdidas gestacionales y la necesidad de más investigaciones para determinar el impacto de estas alteraciones en la viabilidad del embarazo y en el asesoramiento genético.

PALABRAS CLAVE

Cromosoma 13, Delección, Cromosomopatía, Pérdida recurrente del embarazo.

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Introduction

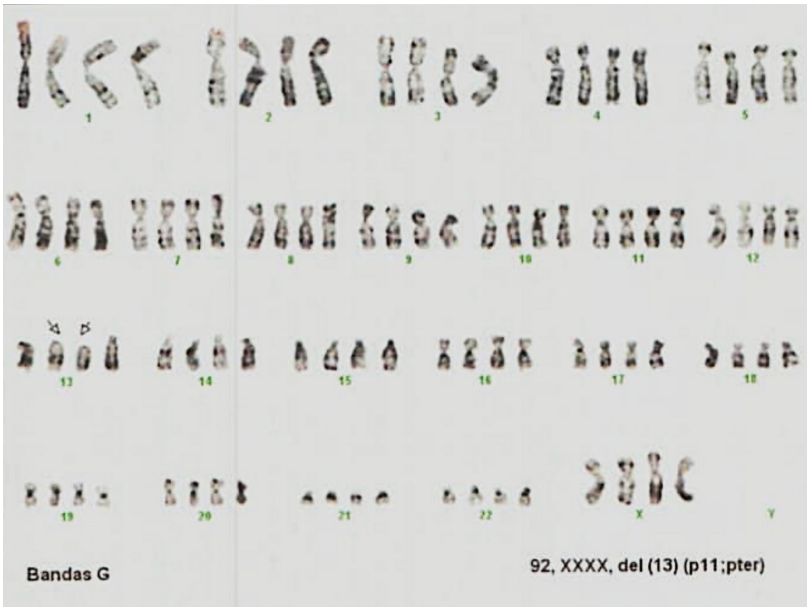
Chromosomes are structures made up of a properly packaged Deoxyribonucleic Acid (DNA) molecule in an orderly manner through proteins known as histones. This complex structure primarily functions as a carrier of genetic material, contributing to the formation of the genome and facilitating the transmission of genetic code from one generation to the next.[1,2] During the transfer of material information from one cell to another in processes known as mitosis or meiosis, alterations at the chromosome level may occur, which can be numerical or structural.[2]

According to the above, structural chromosomal alterations are those changes in the chromosome secondary to a break, rearrangement, or fusion between chromosomes, either within the same chromosome or between several. Among these alterations, we can find modifications due to the loss of a chromosomal section that may involve one or several bases, even compromising a gene fragment, known as deletion. Likewise, there are orientation changes in a segment, called inversion, as well as alterations characterized by an exchange of segments between two chromosomes, defined as translocation (reciprocal or Robertsonian). These alterations, depending on their location and type, can lead to pathological phenotypes.[2]

Although chromosomal disorders have been directly linked to congenital defects in up to 8 % of live births and up to 28 % of neonatal deaths and stillbirths,[3] most of these structural alterations are sporadic or de novo, meaning they are not inherited from the parents as they arise randomly. Additionally, these alterations are associated with predisposing factors such as parental age or environmental factors.[4]

It is worth noting that structural alterations in acrocentric chromosomes, having a long arm that houses protein-coding genes while the short arm lacks unique coding sequences, generally do not have clinical relevance. Similarly, deletions affecting this region are uncommon, and even rarer are those with a hereditary pattern. Therefore, this article describes a case of a microdeletion in the short arm of chromosome 13, observed in both a twin pregnancy and the mother.[5]

Figure 1
F1: 92, XXXX, del (13) (p11, pter)



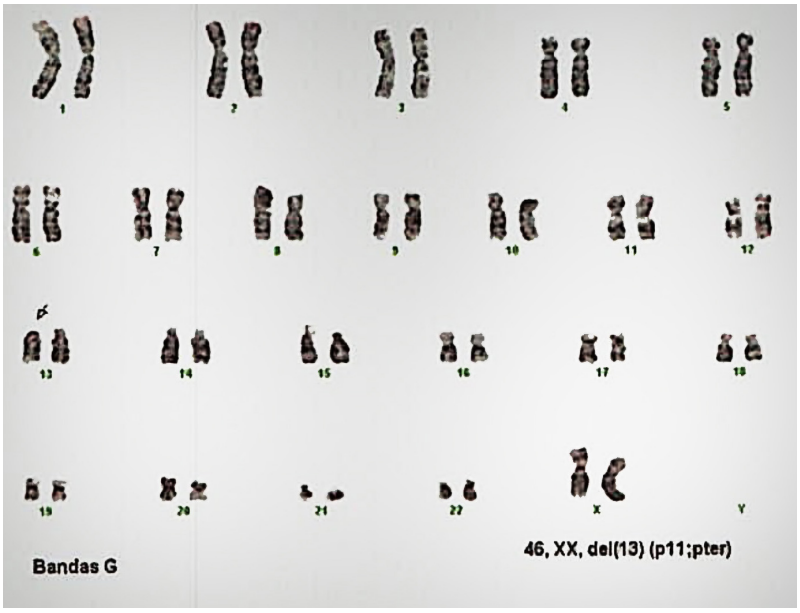
Karyotype showing tetraploidy and deletion of the short arm (p) of chromosome 13, with telomere breakpoints (p11; pter).

Methodology and Results

A 37-year-old pregnant woman, at 22 weeks of gestation and with a history of recurrent pregnancy losses, was referred by her gynecologist-obstetrician for a genetic counseling consultation to undergo cytogenetic studies due to the fetal demise of one of the fetuses in her current pregnancy. With a multidisciplinary approach, a retrospective descriptive study of the medical history was conducted to identify the cause of the inherited microdeletion in the short arm of chromosome 13 in a twin pregnancy with manifestations of heteromorphic chromosomes.

As part of the methodology, a fetal karyotype was performed through chorionic villus sampling (CVS), identifying a karyotype of 92, XXXX in fetus

Figure 2
F2: 46, XX (13) (p11; pter)



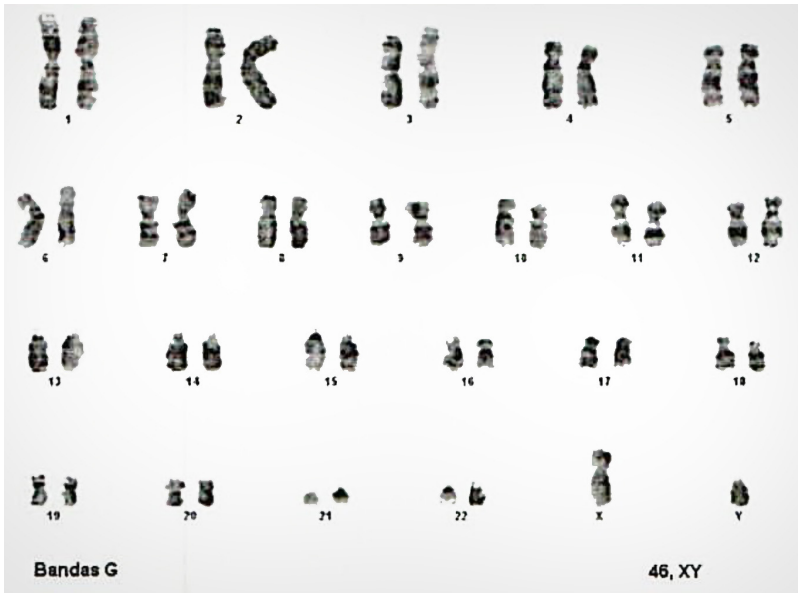
Karyotype showing the deletion of the short arm (p) of chromosome 13, with telomere breakpoints (p11; pter).

1 (F1) (Figure 1) and a karyotype of 46, XX in fetus 2 (F2) (Figure 2). In both fetuses, the presence of a deletion in the short arm of chromosome 13 was observed.

Karyotype showing the deletion of the short arm (p) of chromosome 13, with telomere breakpoints (p11; pter).

Following these findings, cytogenetic studies were conducted on the parents using venous blood samples. The father's analysis revealed a normal karyotype (Figure 3), while the mother's study showed the same deletion observed in the offspring, without other significant cytogenetic alterations (Figure 4). These results suggest a possible hereditary pattern of the maternal microdeletion and highlight the importance of cytogenetic studies in evaluating reproductive disorders associated with structural chromosomal abnormalities.

Figure 3
Father: 46, XY



Normal karyotype.

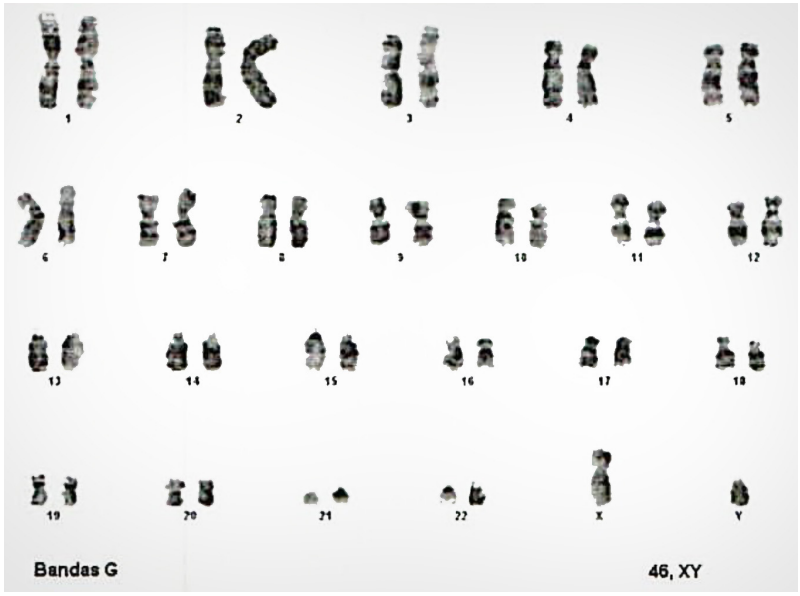
Discussion

The human karyotype consists of 46 chromosomes organized into 23 pairs, of which 22 are autosomal and one pair comprises the sex chromosomes (XX in females and XY in males). Each chromosome has a structure composed of two arms: the short arm (p) and the long arm (q), separated by a centromere that defines its morphology.[6] Chromosomal structural alterations can occur through various mechanisms, resulting in deletions, duplications, translocations, inversions, or ring chromosomes, leading to different genetic disorders. Structural abnormalities can be classified as balanced and unbalanced. The former do not involve the gain or loss of genetic material and can be inherited without an evident phenotype, whereas the latter involve the loss or gain of chromosomal segments, which may cause congenital diseases or specific syndromes.[7]

Among these alterations, deletions are characterized by the loss of a DNA segment, with severity varying depending on the extent and location of the missing material. This loss generates monosomy in the affected region and can present in different ways. When a chromosome undergoes a single break, a terminal deletion occurs, with the exposed end stabilized through the incorporation of telomeric repeats by telomerase or through cryptic translocations. In contrast, if two breaks occur in the same chromosomal arm and the resulting ends fuse, an interstitial deletion is formed. These deletions can occur in isolation or together with the duplication of another chromosomal segment, as seen in unbalanced reciprocal chromosomal translocations. This phenomenon is often a consequence of abnormal segregation or defective crossing-over in individuals carrying a translocation or inversion.[7,8]

Chromosome 13 is one of the five acrocentric chromosomes (13, 14, 15, 21, and 22). Its long arm contains most of its genes, whereas its short arm consists of three regions: the

Figure 4
Mother: 46, XX (13) (p11; pter)



Karyotype showing the deletion of the short arm (p) of chromosome 13, with telomere breakpoints (p11; pter).

distal portion of the short arm, the nucleolar organizer region (NOR), which contains ribosomal RNA-coding DNA, and the satellites.[9,10] Although satellites have been considered structures of secondary relevance, a possible association, still not fully confirmed, has been proposed between abnormalities in these regions and various diseases such as cancer,[11] recurrent pregnancy loss, infertility, and even some aneuploidies.[12,13]

The deletion observed in the short arm of chromosome 13 in the mother and her fetuses could be associated with an underlying chromosomal rearrangement, possibly a Robertsonian translocation.[14] These translocations occur when two acrocentric chromosomes, such as chromosome 13, fuse their long arms at the centromeric region, resulting in the loss of the short arms. More cases of specific syndromes associated with alterations in the long arm of chromosome 13 than in the short arm have been reported in the literature. This is because chromosome 13 is acrocentric, and its short arms contain only ribosomal RNA genes, making their absence rarely clinically significant.[15,16]

Although carriers of Robertsonian translocations are typically phenotypically normal, they have a higher risk of producing unbalanced gametes, which may lead to chromosomal abnormalities in their offspring. In this context, the deletion detected in the fetuses and shared with the mother suggests the presence of a preexisting chromosomal rearrangement in her, indicating a possible hereditary pattern. This structural alteration could have contributed to the patient's recurrent pregnancy losses,[14] likely due to chromosomal segregation errors during meiosis.[16]

Conclusions

The case presented is an example of a rare manifestation of chromosomal heteromorphism. Despite having a deletion in the short arm of acrocentric chromosomes, particularly chromosome 13, these findings are unusual and lack clinical significance. However, the presence of this deletion in both the mother and her offspring suggests a hereditary pattern that could be implicated in recurrent pregnancy loss. Given the limited number of studies available in the literature regarding clinical outcomes associated with deletions in the short arms of acrocentric chromosomes, particularly chromosome 13, expanding research in this area is essential. Future studies could clarify the impact of these alterations on pregnancy viability and potential phenotypic consequences. A better understanding of the relevance of these structural alterations will allow for the optimization of genetic approaches in patients with a history of recurrent pregnancy loss and contribute to the development of more precise diagnostic and reproductive strategies.

Conflict of Interest

The authors declare no conflicts of interest related to the study topic.

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