PRE356

A novel report of multigenerational chromosome 16 centric fission

Sidney VanDyke-Ries, MS, LCGC;[1] Ellen Parker, MS, LCGC;[1] Stephanie Kramer, MS, CGC;[2] Judith Knops, PhD, FACMG;[1] Armine Mendivil, BS[1]
[1]Labcorp Genetics and Women's Health, Labcorp, Santa Fe, NM; [2]University of Kansas Health System, Kansas City, KS

1. Introduction

Centric fission occurs when a centromere separates, resulting in two new stable chromosomes. Examples of centric fission have been detailed in the literature across many species; however, cases reported in humans are limited. Here we document a multigenerational inheritance of 16p and 16q telocentric chromosomes derived from a centric fission.

2. Methods

A chorionic villus sample was submitted to Labcorp for chromosome analysis. A total of 20 metaphases from 2 separate cultures were examined, of which 5 were analyzed and 3 were karyotyped at a 450 band resolution. Clinical information and family history were provided by the ordering genetic counselor.

3. Case Report

A 36-year-old, G6P1SAB4 patient sought genetic counseling and elected prenatal diagnostic testing due to a known family history of chromosome 16 centric fission. The patient's mother has a history of pregnancy loss and a 26-week gestation pregnancy with multiple anomalies and an unbalanced karyotype. The patient's mother subsequently elected chromosome analysis, which identified the chromosome 16 fission [47,XX,-16,+fis(16)(p10),+(16)(q10)]. The patient's mother presents with a normal phenotype. Medical records noted that "she is in good health" and "has suffered no secondary mental or physical handicap".

The patient was diagnosed prenatally to carry the same fission and has a normal phenotype (**Figure 1**). The patient has been seen by several genetic counselors and her primary OBGYN did not list any concerns of physical or intellectual disability. The patient had four miscarriages and one full term pregnancy, which resulted in a daughter with the same fission and a normal phenotype. There are no records of the patient's mother, patient, or patient's daughter undergoing a physical evaluation by a geneticist.

Chromosome analysis of the patient's current pregnancy detected the same centric fission (**Figures 2 & 3**). This pregnancy had normal 12- and 20-week ultrasounds and nuchal translucency scan. The baby was subsequently delivered at 39w2d and no concerns were indicated

4. Conclusions

This case of chromosome 16 centric fission details a remarkable example of a phenotypically normal inherited and balanced carrier, as well as the transmission of non-balanced gametes (**Figure 4**). It is important to note that centric fission carriers may be referred to genetic counseling due to a history of recurrent miscarriage. Parental chromosome analysis can detect these centric fissions, if present, which is commonly recommended for recurrent miscarriage. Detection of a centric fission carrier could provide an explanation for families where recurrent miscarriages were previously unexplained. Additionally, knowledge of centric fission is important for pediatric genetic counselors who may see the offspring of individuals who carry the balanced complement. To our knowledge, this case report is the first to detail a multi-generational transmission of chromosome 16 centric fission and contributes to the overall limited literature available regarding centric fission.

Figures

Figure 1. Patient's peripheral blood chromosome analysis.

MEDICAL GENETICS REPORT (continued)

MEDICAL GENETICS FINAL

Collection Date: XX/XX/XXXX Case: XXXXXXXXX

CHROMOSOME ANALYSIS
47, XX, -16, +fis(16)(p10),+fis(16)(q10)
Peripheral Blood

INTERPRETATION: Abnormal female karyotype showing centric fission of chromosome 16 in which there is a break in the centromere of one copy of chromosome 16 resulting in two derivative chromosomes, one composed of the short arm and one composed of the long arm.

Centric fission leads to the formation of two stable telocentric chromosomes. While such an event rarely occurs in humans, it has been implicated in the evolution of eukaryotic karyotypes (Perry J et al., 2004). First described by Sinha AK et al. in 1972, it has been subsequently documented in chromosomes 4, 7, 9, 12, and 21.

Although this configuration is stable in this individual, there is a high risk of transmission of non-balanced gametes resulting in chromsomally unbalanced offspring. Genetic counseling and prenatal diagnosis of future pregnancies are strongly recommended.

Figure 2. Chromosome analysis on the patient's CVS sample.

Metaphases Counted:	20			**Banding Technique:**	GTW
Metaphases Analyzed:	5	**Number of Cultures:**	2	**Banding Resolution:**	450
Metaphases Karyotyped:	3	**Subculture:**	N	**Dept. Section:**	POCCVS

RESULTS: 47,XX,-16,+fis(16)(p10),+(16)(q10)
Female karyotype

Figure 3. Karyotype on the patient's CVS sample.

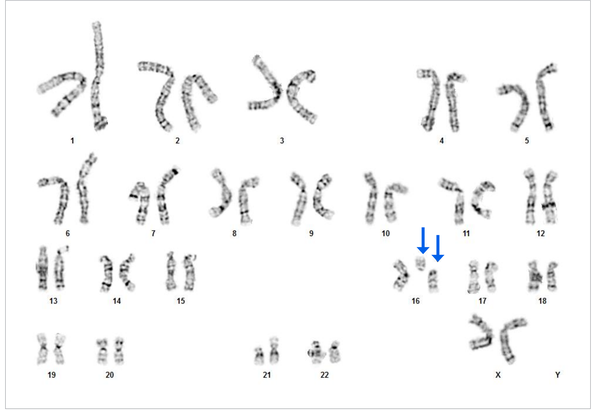
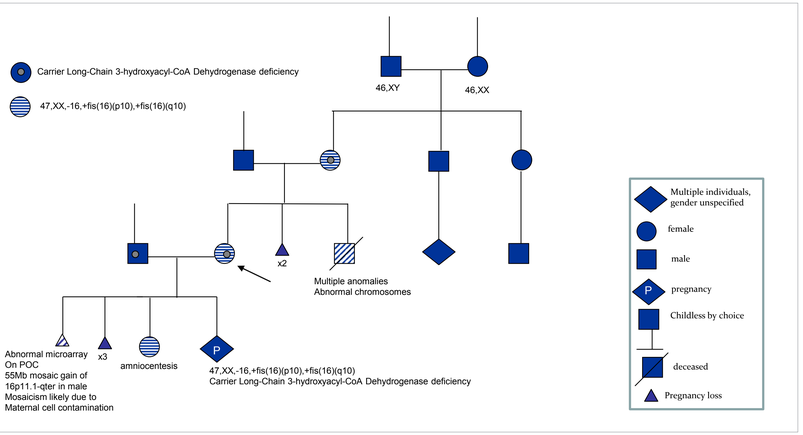


Figure 4. Patient's pedigree.



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