Premature Centromere Division and Spontaneous Abortion

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ARTICLEINFO

Article Type:
Case Report

Article History:
Received: 6 Feb 2013
Revised: 15 Feb 2013
Accepted: 15 Feb 2013

Keywords:
Cell Division
Chromosomes
Chromatids
Premature Centromere Division
non-Disjunction
Abortion

ABSTRACT

Background: Premature Centromere Division (PCD) was observed in the chromosomes of metaphase spreads in a patient with the history of recurrent abortions.

Case Report: Short term leukocyte cultures were set up with blood sample from the woman with a history of recurrent abortions for the past four consequent years. 25 % of the metaphase spreads screened displayed premature centromere division of the chromosomes in each of the cells.

Conclusion: This abnormal behavior of the centromeres may predispose the individual to cell division errors due to chromosome instability and the consequences of which may be a spontaneous abortion.

►*Implication for health policy/practice/research/medical education:*
Premature Centromere Division and Spontaneous Abortion

► *Please cite this paper as:* Govindasamy R, Murali N, Anand G, Shastri D, Rajitha V, Selvi P, Kumar-Babu S, Anitha MR. *Premature Centromere Division and Spontaneous Abortion*. *International Journal of Medical Toxicology and Forensic Medicine*. 2013; 3(2): 67-70.

1. Introduction:

Cytogenetic investigations have always been a tool in identifying the abnormalities in normal cellular process. Cell division consists of prophase, metaphase, anaphase and telophase. During metaphase the chromosomes are lined up in equatorial plane with spindle fibers attached to centromere to the opposite poles of the cell. Anaphase begins with the division of centromere leading to separation of the chromatids, each of the chromatids disjoin and form daughter chromosomes, which move to the opposite poles of the cell along the spindle fibers. In premature centromere division the separation of the centromere occurs precociously which leads to cell division errors. The premature centromere division of the chromosomes disconnects with spindle fibers which leads to non-disjunction. The individual with these cell division errors are normal but they are considered to be mosaic both in somatic cells and gametes. The individual with premature centromere division in gametes have more chances of

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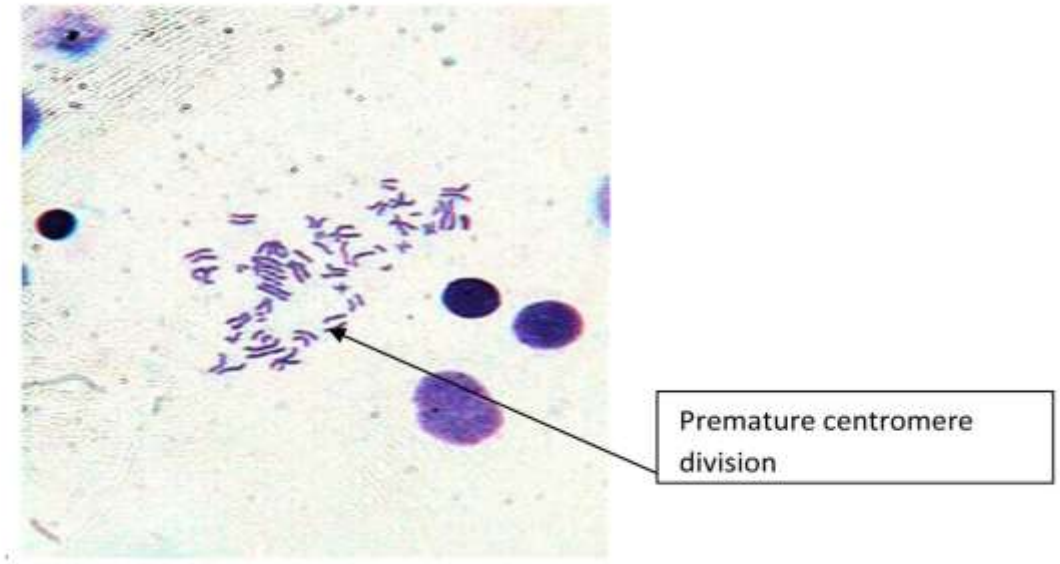

Fig. 1. Metaphase spread displaying PCD (x 1000).

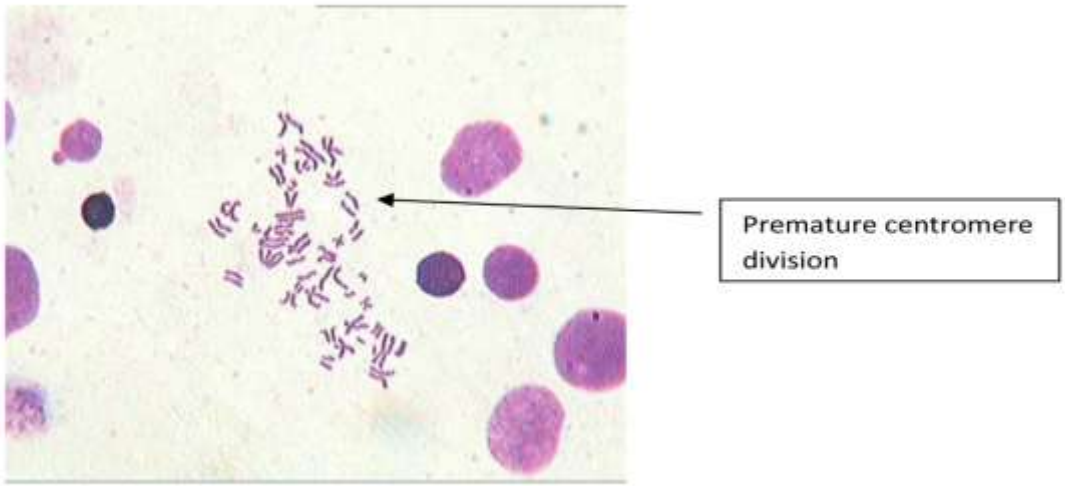

Fig. 2. Metaphase spread displaying PCD (x 1000).

non disjunction which could be a cause for spontaneous abortion.

2. Case Report:

A 26 year woman from West Bengal admitted to the Vinayaka Missions Kirupananda Variyar medical college and Hospital, Salem, Tamil Nadu in Mid of 2012, with the history of recurrent unusual, spontaneous, termination of pregnancy. She married to a man of 37 years old which is a non-consanguineous marriage. Spontaneous abortions were recorded from the year 2005 at 15 weeks of first gestation; at 12 weeks of second gestation during the year 2006; at 9 weeks of third gestation during 2007 and at 17 weeks of fourth gestation by intrauterine fetal death (IUDF); pregnancy termination at 7 weeks of fifth gestation during 2012.

There is no history of recurrent abortions in their family pedigree and her menstrual cycles are regular with dysmenorrhea. Investigation of T3, T4 and TSH along with blood sugar level and routine blood parameter values are found to be normal. Transvaginal sonography shows no definite abnormality. Hence, a cytogenetic examination is carried out in the couple to rule out the chromosomal abnormality.

Cytogenetic investigation

The blood sample was collected from the above mentioned details of woman in a completely sterile heparinized vacutainer tubes and mixed well. The cultures were setup with RPMI 1640 (Roswell Park Memorial Institute) culture medium, Phytohemagglutinin (PHA) and, plasma and buffy coat were added from the centrifuged blood samples .The cultures were incubated at 37.5˚C for 72 hours and arrested with colchicine, 1.5 hour prior to harvest. This was followed by hypotonic treatment with 0.75 M Kcl (potassium chloride) for 30 minutes and fixed in methanol: glacial acetic acid fixative 3:1 ratio. Air dried slides were prepared and stained with 4 per cent Giemsa stain (The AGT cytogenetic Laboratory manual) 3rd edition (1). Differential count of about 100 cells was made for each culture to estimate the mitotic drive and mitotic index. Non over lapping metaphase spreads with appropriate staining were photographed for confirmation.

3. Discussion:

The metaphase spreads of the spouse did not display any structural or numerical chromosomal abnormality. Of the 100 metaphase spreads screened, premature centromere division was observed in 25% of the metaphase chromosomal spreads. A hypothesis was proposed by B.K.Vig (2) (1984) that premature centromere division may result in non-disjunction by impairing the attachment of spindle fibers to prematurely separated centromeres. An increased frequency of premature centromere division was found in lymphocyte cultures from a couple with recurrent spontaneous abortions.

Of the 100 metaphase spreads screened 25% of the spreads displayed (fig. 1 and 2) premature centromere division in the woman. Premature centromere division was observed in all chromosomes in each of the metaphase chromosomal spreads observed in the present case report. Anuradha *et al* (3) (2001) observed Premature centromere division in lymphocyte culture of all the chromosomes, in couples with recurrent spontaneous abortions and it was found that percentage of premature centromere division in couples varied from 9% to 47% in individuals with history of spontaneous recurrent abortion. Whereas in the present case report 25% of the metaphase spreads in all the chromosomes examined displayed premature centromere division in the karyotype of woman alone (fig. 1 and 2).

Premature centromere division in a family of four members reported by Madhan *et al* (4) (1987) showed normal phenotype which could be due to inherited cytogenetic disorder. Bajnoczky *et al* (5) (1993) had reported premature centromere division in couples with history of recurrent abortions. Kalpana *et al* (6) (2004) reported spontaneous abortions in a female aged 26 years with premature centromere division. All individuals with premature centromere division displayed normal chromosomal complement of 46 XY and 46 XX. A study done by S. Mustaqahmed *et al* (7) in 30 women who experienced recurrent pregnancy loss and observed Premature centromere division and 20.5 % cells with Premature centromere division viewed as a manifestation of chromosome instability.

Increased frequency of mitosis showing premature centromere division was reported in four members of a sub-fertile family by Gabarnon *et al* (8) (1986). FISH (fluorescent in situ hybridization) study in premature centromere division done by Alfredo *et al* (9) (2005) showed the presence of alpha satellite DNA from

chromosomes 1, 13, 21/18, X, all centromeres, and centromere protein [CENP-B] box sequences in metaphasic and anaphasic cells from PCD individuals [CENP-B] plays fundamental role in function of centromere chromatin Yoshinao Muro *et al* (10).

The result of the present case report and the review of literature reveal that the abnormal behavior of centromeres manifested as premature centromere division is a mechanism of non-disjunction and it involves all chromosomes in a cell which could lead to aneuploidy with consequences of spontaneous abortion.

4. Conclusion:

The present case report clearly manifest that premature centromere division is the error of cell division (Chromosomal instability) that has occurred in the metaphase precausiously. Premature centromere division could also been influenced by the environmental factors. This study points out the importance of karyotyping in couples experiencing recurrent abortions for their genetic testing and genetic counseling. FISH (Fluorescent in situ hybridization) studies should be done to find out the structural constitutive components of DNA at the centromere.

References

1. Margaret J, Jack L, Spurbeck BS. The AGT cytogenetic Laboratory manual 3rd edition. Peripheral blood cytogenetic method: Lymphocyte macro culture.91-93.
2. Vig BK. Sequence of centromere separation another mechanism for the origin of non-disjunction. Hum Genet. 1984;66:239-243.
3. Anuradha M. Manjunatha Premature Centromeric Division and Abortions. IJHG. 2001;1(3):191-193.
4. Madhan K, Lindhout K, Palan A. Premature centromere division PCD: A dominantly inherited cytoxzgenetic anomaly . Hum Gene. 1987;77:193 -196.
5. Bajnoczky K, Gardo S. Premature anaphase in a couple with recurrent miscarriages Hum Genet. 1993;92:388-390.
6. Lakshmi Kalpana V, Satyanarayana M, Prabhaker S, Sarvani R. Chromosomal Instability in Recurrent Spontaneous Aborters. Int J Hum Genet. .2004;4(1):31-36 .
7. Mustaqahmed S, Balachander V, Mohanadevi S. Identification of cytogenetic alterations in infertile couples experiencing repeated spontaneous abortions using Giemsa Trypsin Giemsa banding (GTG). Scientific research and essays. 2011;6(1):182-186.
8. Gabarrón J, Jimenez A, Glover G. Premature centromere division dominantly inherited in a sub fertile family. Cytogenet Cell Genet. 1986;43:69-71 .
9. Corona-Rivera A, Salamanca-Gomez F. Cell cycle and centromere FISH studies in premature centromere Division. BMC Medical Genetics. 2005;6:33-37.
10. Muro Y. Centromere Protein B Assembles Human Centromeric a-satellite DNA at the 17-bp Sequence, CENPB Box. The Journal of Cell Biology. 1992;116:585-596.