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Premature Centromeric Division and Abortions

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KEY WORDS Recurrent spontaneous abortions; premature centromere division. also performed as described by Eiberg (1974).

ABSTRACT An increased frequency of mitoses with centromere separation affecting all chromosomes was found in lymphocyte cultures of couples with recurrent spontaneous abortions. This anomaly was recorded in six individuals out of seventy couples (one hundred and forty individuals) with recurrent miscarriages. The abnormal behaviour of centromeres may predispose the individual to cell division errors, the consequence of which may be a spontaneous abortion.

INTRODUCTION

It has been reported earlier that the centromere division of human mitotic chromosomes is nonrandom and that a "normal sequence" of centromere separation exists (Vig and Wodnitzki 1974; Mehes 1975; Meher et al. 1981; Vig 1981; 1983; Bajnocyky et al. 1983). Repeated spontaneous abortions may be caused not only by balanced translocation, but also other chromosomal abnormalities including centromere anomalies, that predispose to meiotic non-disjunction. (Murthy et al. 1990; Rudd et al. 1983). In the present study, we report on high number of mitoses with centromere separations of all chromosomes in couples with recurrent miscarriages.

MATERIALSAND METHODS

Seventy couples who were referred for chromosomal studies because of recurrent spontaneous abortions were studied after all other possible etiological factors causing abortions were rules out.

Chromosome studies were carried out on Gbanded lymphocyte cultures from the couples. Peripheral Blood lymphocytes were cultivatged in RPMI 1640 medium, supplemented with 15% fetal calf serum and phytohaemagglutinin. Termination and slide preparation was done according to standard protocols Cd-Banding was

RESULTS

Premature centromere division (PCD) of all chromosomes (Fig.1) was found in 9% to 47% of cells in three males and three females. Table 1 represents the frequency of PCD among the abortes couples. It is also seen from the table that the percentage of PCD cells are more in the individuals with a chromosomal abnormality when compared to the individuals with normal karyotypes.



Fig. 1. Metaphase showing premature centromeric division

DISCUSSION

Chromosome studies in the positive cases reaveled the presence of completely normal metaphases or PCD cells.PCD has been described by Fitzgerald (1975),GALLOWAY AND Buckton (1978) in aged woman in association with aneuploidy of X-chromosome.Vig (1984) proposed a hypothesis that PCD may result in nondisjuction by impairing the attachment of prematurely separated centromeres to spindle fibers. Miller et al. (1990) reported association of

Table 1:	Percenta	ige of p	rematu	ire	centromeric
	division	(PCD)	cells	in	lymphocyte
	cultures	observed	l in the	pr	esent study

Case No.	Sex	Nunber of of abortions	% of PCD cells	Karyotype
22	F	2	9	46, XX
34	F	2	16	46, XX
46	F	1	47	46, X del (q 28 \rightarrow qter)/46 XX
50	М	2	23	46, XY q+
45	М	2	21	46, XX
58	Μ	2	17	46, XY

PCD with various aneuploidies in a high percentage, supporting a functional relationship between disturbances in the mechanism of centromere separation and chromatid separation at cell division.

An increased frequency of mitoses with centromere separation affecting all chromosomes was found in lymphocyte culture from a couple with recurrent spontaneous abortion reported by Bajnoczky et al. (1993) who concluded that patients with altered centromere functions may have an increased risk for chromosomes instability and that the abnormal behaviour of centromere may predispose the individual to cell division errors; the consequence of which may be a spontaneous abortion. Bajnoczky and Meher (1988) studied the centromere separation of four infants with trisomy 18, five patients with trisomy 21 and five children with normal Karyotype. "Late separtion" of chromosome 21 in three mothers and in one father of four children with trisomy 21. No out-of-phase separation occurred in the mitoses of the parents of normal children. These findings confirm the assumption that at least in some of the cases the out of phase centromere separation of a given autosomes is related to the aneuploidy of the same chromosomes in off spring.

Increased frequency of mitoses showing PCD was reported in four members of a subfertile family by Gabarnon et al. (1986). The authors conclude that if abnormal behaviour of the centromere on the X-chromosomes, manifested as PCD is the mechanism of non-disjunction responsible for X-chromosome aneuploidy it seems logical to presume that if PCD involved all chromosomes in a cell, it could lead to increased aneuploidy for different chromosomes, with the consequences of recurrent spontaneous abortions.

Murthy and Prabhakara (1990) reported a female with history of spontaneous abortion and subsequent birth of Downs Syndrome child. Her chromosomal analysis revealed 46, XX with pericentric inversion of 9qh, while her husband's was normal. Metaphase analysis of the female showed 20.5% cells with premature centromere divisionl, 4% cells with endoreduplication and 2% with polypolidy. These frequencies were considerably higher as compared to a normal control. They concluded that inv (9qh) might have some inter chromosomal effect leading to higher incidence of mitotic disturbances finally resulting in aneuploidy. This predisposition is evident by spontaneous abortion and down syndrome child.

Similarly in the present study it is observed that PCD cells are more in the individuals with chromosomal abnormality when compared to the individuals with normal karyotype.

Thus, the observation in the present study shows that patients with altered centromere functions may predispose to cell division errors due to chromosome instability and thus may lead to spontaneous abortions. Such a correlation awaits a better understanding of the nature of these cytogenetic observations and the events controlling mitosis and meiosis at the molecular level.

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