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Satellite Associations in Recurrent Aborters

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ABSTRACT The frequency and pattern of satellite association was studied in lymphocyte culture of couples with recurrent spontaneous abortions and control population. A statistically highly significant increase of the satellite association frequency among the aborter couples has been observed in comparison to the control group ($P < 0.001$). The role of satellite association in non-disjunction is discussed.

INTRODUCTION

The phenomena of satellite association (SA) involving a specific position of the satellite chromosomes with their satellite directed towards each other was first observed in mitotic human chromosomes. (Ferguson Smith and Handmaker 1961; Ohno et al. 1961) and was found also in meiotic chromosomes (Ferguson-Smith 1964). The formation of SA's has often been attributed to the involvement of satellite chromosomes in nucleolar formation. The sticky nucleolar material would have a tendency to hold the associated chromosomes together through mitosis (Hsu et al. 1965).

The fusion of two or more nucleoli would tend to stretch mechanically the nucleolar forming chromosome segment with obvious risk of breakage. If breaks occur in more than one of the chromosomes involved the closeness of the broken ends would predispose to translocations and the SA would thus be active also in the origin of translocation between satellite chromosomes. A high incidence of SA has often been considered as predisposing to a increased tendency of non-disjunction in satellite chromosomes and thus to the induction of D and G trisomies.

MATERIALS AND 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 ruled out.

Chromosome studies were carried out on G-banded lymphocyte cultures. The criteria for evaluating acrocentric association was as described by Hansson (1970). The tendency of the individual satellite chromosomes to be involved in satellite association (SA) are indicated in the association Index (AI = the number of associated chromosomes of a specific type divided by the total number of the type). Thirty metaphases were scored to note the SA frequency.

The following formula was used to know the differences in the samples for each acrocentric chromosome.

$$t = \frac{\left|\overline{X}_1 - \overline{X}_2\right|}{\sqrt{\frac{n_1\sigma_1^2 + n_2\sigma_2^2}{n_1 + n_2 - 2}} \times \sqrt{\frac{1}{n_1} + \frac{1}{n_2}}}$$

Where

$\overline{X}_1$ = mean associating index of sample 1
$\overline{X}_2$ = mean associating index of sample 2
n_1 = number of individuals in sample 1
n_2 = number of individuals in sample 2
σ_1 = Standard deviation of sample 1
σ_2 = standard deviation of sample 2.

RESULTS

A statistically highly significant increase of the satellite association frequency among the aborter couples was observed in comparison to the control group. ($P < 0.001$).

The mean AI's (association indices) and the standard errors of female subjects and controls and also of male subjects and control are given in table 1. The mean AI's were subjected to t-test. Significant was found for chromosome 21, 13 and 15. Metaphase plate with SA is represented in figure 1.

Analysis of Satellite Association Complexes

In general there are fifteen types of associations possible involving all the five different acrocentrics. A high frequency of all types of associations has been recorded in the subjects when compared to the controls. The most frequent association pair was 13-14 of DD type 13-21 followed by 14-21 of DG type and 21-22 of GG type. Among these acrocentric 21 and 13 were most frequently involved in association.

Table 1: The mean association Index (AI's) of the acrocentrics in study group and controls

Chromosome number	Study group		Controls		
	mean ± SE	95% CL	mean ± SE	95% CL	
			Female		
13	0.109 ± 0.006	0.115 - 0.103	0.060 ± 0.006	0.066 - 0.054	4.2**
14	0.083 ± 0.008	0.091 - 0.075	0.061 ± 0.007	0.068 - 0.054	1.61
15	0.057 ± 0.005	0.062 - 0.052	0.032 ± 0.003	0.035 - 0.029	2.89*
21	0.127 ± 0.008	0.135 - 0.119	0.075 ± 0.01	0.085 - 0.065	3.52**
22	0.071 ± 0.006	0.077 - 0.065	0.054 ± 0.005	0.059 - 0.049	1.71
			Male		
13	0.100 ± 0.007	0.107 - 0.093	0.046 ± 0.005	0.051 - 0.041	4.5**
14	0.081 ± 0.008	0.089 - 0.073	0.067 ± 0.007	0.074 - 0.06	1.05
15	0.063 ± 0.005	0.068 - 0.058	0.028 ± 0.016	0.044 - 0.012	4.3**
21	0.109 ± 0.006	0.115 - 0.103	0.075 ± 0.008	0.083 - 0.067	2.9*
22	0.063 ± 0.004	0.067 - 0.059	0.052 ± 0.005	0.057 - 0.047	1.46

* P < 0.01 ** P < 0.001 CL – Confidence limit SE – Standard Error

DISCUSSION

Satellite association and non-disjunction:- One third of trisomies observed in spontaneous abortions and live borns involve acrocentric chromosomes (Hassold and Jacobs 1984), it has been proposed that the presence of NORs on the short arms of all five acrocentric chromosomes predispose them to non-disjunction. (Polani et al. 1960; Mirre et al. 1980; Schmickel et al. 1985; Garcia et al. 1989).

Severl papers have reported evidence of an increased SA tendency in mothers of Downs syndrome children (Hansson and Mikkelsen 1974; Mattei 1974). The idea that high satellite association (SA) tendency may influence the risk of non-disjunction was strongly supported by the fact that the SA tendency of chromosome 21 of the parents with non-disjunction was significantly increased when compared with a control group as studied by Hansson and Mikkelson (1976, 1978).

Galperin et al. (1980) studied acrocentric associations in male and female cells and found that acrocentric 21 and 13 were most frequently involved in associations. They concluded that these tendencies to associate might be related to the reported frequencies of non-disjunction.

In a study conducted by Hansson (1979) a strongly significant increase of the association

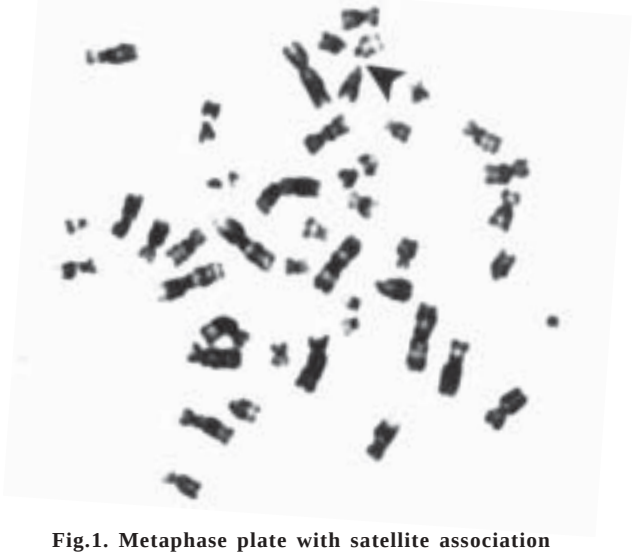

Fig.1. Metaphase plate with satellite association

index (AI) of chromosome 21 in mothers of Down syndrome indicated that SA tendency will influence the risk of non disjunction. The idea was further supported by the results in the families with two DS patients in whom the SA tendency of chromosome 21 was highly increased In addition the high AI of chromosome 21 also increased the indices of the other acrocentric involved in the same association complex.

It was also found that in the present study chromosome 21 and 13 had the highest values of number association in couples with recurrent abortions when compared to the controls which may increased the risk of non-disjunction.

The frequency and pattern of acrocentric chromosome associations in reproductive outcomes has been studied by Anitha and Coworkers (1997) who have reported a higher incidence of acrocentric chromosome associations in both partners experiencing two or more recurrent miscarriages. They suggested that acrocentric chromosme associations are highly relevant because most aneuploidic conceptuses results from meotic non-disjunction during gametogenesis.

Most likely, SA's and fusions of nucleoli are different manifestations of the same phenomenon and acrocentrics belonging to one association complex will organized a common nucleolus. Consequently, two frequently associated aerocentrics are more likely to be involved in translocations with each other. Mikkelson et al. (1975) thus found a significant increase of 13-21 (and 13-15) associations in a mother (with a normal constitution) of a t(13q 21q) carrier. Studies of fluorescent variants indicate that the translocation originated from the mother.

It has been reported by several investigators that most translocations in DS families are between chromosome No.14 and 21. Hansson and Mikkelson (1975) found that in the case of balanced D/G translocation carriers at least one of the parents (with a normal chromosome constitution) had an increased tendency to SA's between the types of chromosomes involved in the translocation in the next generation.

Chromosomes frequently involved in the association complex should have a tendency to form Robertsonian translocation with each other than with chromosomes which are rarely found in the same S.A complex. Jacobs et al. (1974) analysed the distribution of acrocentrics involved in Robertsonian translocations in non-disjunction and demonstrated an excess of t (Dq Dq) and a deficiency of t (Dq Dq) and t (Gq Gq). Further more, the involvement of acrocentrics in each group was non-random. Thus, there is an excess of t(13q 14q) as compared with their translocations among D group chromosomes,. Similar investigations have shown that t(14q 21q) is the most frequent translocation involving D and G group chromosomes. In all types of individuals studies the most frequent DD association was between chromosomes 13-14 and the most frequency DG Association was between chromosomes 14 and 21. These results are in agreement with the non-random involvement of acrocentrics in Robertsonian translocations. The same trend of significantly increased associations of 13-14 and 14-21 also been documented in the present study in a high proportion when compared to the control population.

In the present study there was significant increase of satellite associations in the aborter couples. Chromosomes 13, 21 and 15 showed a significant frequency of number associations. Thus the high frequency of satellite associations in these couples could predispose them to non-disjunction and the results seem, consistent with the hypothesis that acrocentric associations are related with non-random distribution of acrocentric non-disjunction and translocations.

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