Cytogenetics in Recurrent Abortions
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Abstract:
The present study comprised of 40 couples with bad obstetric history. Aim of the study was to find out whether any specific chromosomal abnormalities exist in couples with recurrent abortions. Karyotyping with ‘G’ banding was done. The study revealed that, out of 80 positive metaphases, chromosomal anomalies were seen in 3 cases (3.75%). The abnormal karyotypes seen were 45XX,t(21;21), 45XY,t(13;21), 45XY,t(15;15). These translocations are known as Robertsonian translocations, which occur between D and G group of chromosomes.

Key Words: Recurrent abortion, Translocation, Chromosomal aberrations.

Introduction:
Recurrent abortion is defined as the occurrence of three or more consecutive spontaneous abortions. Cytogenetic study should be considered after 2 spontaneous pregnancy losses have occurred (Sider et al, 1988). The importance of recurrent abortion lies not only in the number of lives lost but also the psychic trauma, injury and occasional mortality, which results from this cause. If there is history of previous abortions, it is likely that chromosomal aberrations will be found with greater frequency in them. Various chromosomal abnormalities like reciprocal translocation, centric fusion and mosaicism have been reported in cases with recurrent abortions. Schmid (1962) was the first to report the chromosomal abnormality in recurrent abortion cases.


The present study was designed to see the incidence of chromosomal abnormalities and whether any specific abnormality exist in couples with repeated spontaneous abortions.

Material & Methods:
The present study was carried out on 40 couples attending Gynaecology OPD, with a history of two or more spontaneous abortions. One ml of venous blood was drawn for lymphocyte culture under complete aseptic precautions in a heparinized syringe. It was then added to the culture medium consisting of RPMI 1640 media, triple distilled water, fetal calf serum, phytohaemagglutinin M and antibiotics.

Culture bottles were incubated at 37°C for 72 hrs. Colchicine was then added to the culture bottle to arrest mitosis. At 69th hour it was centrifuged at 1000 RPM for 10 min. Ten ml of 0.075M(0.56%) potassium chloride (KCl) prewarmed at 37°C was added to the above tubes and incubated for 30 min. Recentrifugation was done at 500 RPM for 5 min. The cells were fixed by adding freshly prepared fixative i.e. methanol and glacial acetic acid in the proportion of 3:1. Successive washings with the fixative were given until a colourless material was obtained. Two to three drops of cell suspension was dropped with a pasteur pipette on a wet, chilled (ice cold), grease free slide held at an angle of approximately 30° to facilitate better spreading. Giesma banding was done with Trypsin digestion method (Seabright, 1971).

50 mitotic spreads from more than two slides were screened and observed from every positive sample. Two best spreads from each case were photographed and karyotypes prepared. Individual chromosome identification and reporting was done as per the Paris Report (1971).
Results:

The cytogenetic study was carried out in 40 couples (80 individuals). We observed the chromosomal abnormalities in only three cases. Incidence was found to be 3.75%.

Case 1: A 37 year old female who experienced four first trimester and one second trimester abortions, was referred for chromosomal analysis. She was found to have a 45 XX, t(21;21) translocation. Her husband’s karyotype was normal with no abnormality.

Case 2: A 29 year old female was referred for karyotyping with history of two first trimester abortions. Karyotype was found to be 46 XX and no anomaly was seen. Her husband’s karyotype was found to have 45 XY, t(13;21) translocation.

Case 3: A couple was referred for chromosomal analysis because three pregnancies had ended in first trimester abortions. Karyotype of wife was normal 46XX. But husband was found to have 45 XY, t(15;15) translocation.

Discussion:

Chromosomal aberrations have shown to be a major etiological factor in the occurrence of reproductive loss and fetal wastage. Parents who are carriers of abnormal chromosomes are at higher risk of producing children with chromosomal abnormalities (Carr, 1971).

This study was designed to determine the chromosomal changes in couples with recurrent abortions. The abnormal karyotypes seen in 3 cases were 45 XX, t(21;21) i.e. G/G translocation; 45 XY, t(13;21) i.e. D/G translocation and 45 XY, t(15;15) i.e. D/D translocation. All these translocations were Robertsonian translocations.

In case 1: 45 XX, t(21;21) i.e. G/G translocation was detected in a female. In such a situation, the possible gametes will be either nullisomic or disomic for chromosome 21. Consequently all liveborn children will have Down’s Syndrome. This is one of the very rare situation in which offsprings are at a risk of greater than 50% for having an abnormality. Lewis & Ridler (1977) found a G/G translocation in a woman with a history of recurrent abortion. Maeda et al (1976) demonstrated 22/22 translocation carrier in a woman with recurrent abortions. Farah et al (1975) found a balanced translocation t(22/22) in a woman who had 15 abortions.
Table 1: Showing comparison of present study with other workers.

<table>
<thead>
<tr>
<th>Authors</th>
<th>No. of Cases</th>
<th>Chromosomal abnormalities in percentage (cases)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Schmid (1962)</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Mckay et al (1967)</td>
<td>42</td>
<td>42</td>
</tr>
<tr>
<td>Pergament et al (1968)</td>
<td>39</td>
<td>43</td>
</tr>
<tr>
<td>Kadotani et al (1969)</td>
<td>71</td>
<td>71</td>
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<tr>
<td>Wilson (1969)</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Lucas et al (1972)</td>
<td>42</td>
<td>42</td>
</tr>
<tr>
<td>Papp et al (1974)</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Kim et al (1975)</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Sant-Cassia &amp; Cook (1981)</td>
<td>182</td>
<td>182</td>
</tr>
<tr>
<td>Present study</td>
<td>40</td>
<td>40</td>
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In case 2: One parental balanced D/G (13;21) translocation was observed. In a phenotypically normal individual with a translocation between 13 and 21 chromosome, six possible outcome from such fertilization are: Down’s Syndrome, normal 13/21 carrier, normal progeny, monosomy 21, monosomy 13 and trisomy 21. The last three out come are incompatible with life and could result in abortion. This could explain previous spontaneous abortions in this case. Account of recurrent abortions attributable to D/G translocation have been reported by other workers. (Kuliyev, 1969; Kim et al, 1975; Byrd et al, 1977; Sant-Cassia & Cooke, 1981).

Kim et al (1975) studied a series of 50 couples with recurrent abortions. One woman was found to be mosaic for 45 X / 46 XX / 47 XXX. Three women were found to be balanced translocation carriers, with one having D/G translocation. Sant-Cassia & Cook (1981) carried out chromosomal banding studies on both the partners of 182 consecutive couples with two or more spontaneous abortions. Seventeen abnormal karyotypes were detected including D/G and D/D translocation with frequency of 4.67%.

In case 3: D/D translocation was detected in male with karyotype 45 XY, t(15;15). Lucas et al (1972) described a carrier with D/D translocation involving both number 15 chromosomes. In such a case, a gamete could only receive both the number 15 chromosomes involved in translocation or none of them. On fertilization the resulting zygote would be either trisomic or monosomic for chromosome 15. As neither product was compatible with viability, every pregnancy ended in abortion.

Accounts of recurrent abortions attributable to D/D translocation have been reported by Stenchever et al (1968), Pergament et al (1968), Mennuti et al (1978) and Neu et al (1979).

Stenchever et al (1968) found only one patient with a D/D translocation carrier out of 36 couples and 5 individuals. Pergament et al (1968) studied 39 couples and 4 women who had experienced repeated spontaneous abortions and stillbirths and found one mother with a translocation, which proved to be a D/D translocation. In present work the total frequency of chromosomal aberrations in couples with recurrent spontaneous abortions studied was 3.75 %, almost similar findings were observed by Papp et al (1974), Kim et al (1975) and Sant-Cassia & Cook (1981).


Although the small sample size in this study may not warrant generalization, the incidence of chromosomal abnormalities reported here correlates with that found by other research workers (Table 1).

Since chromosomal anomalies have been recognized as a major cause of early spontaneous abortions, therefore, routine chromosomal banding studies are recommended and justified for both the partners, with repeated spontaneous abortions in absence of any apparent cause.

Bibliography: