REPEATED FETAL LOSS IN REFERRED CASES: A STUDY ON 14 COUPLES WITH SPONTANEOUS ABORTION

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SUMMARY

Selected 14 couples with a history of more than two consecutive abortions were investigated for cytogenetic study. Out of these 14 cases studied, 3 females showed abnormal karyotype as follows.

1. **Mosaic 45, X/46, XX.**
2. **Mosaic 46, XX/46, XY.**
3. **Balanced Robertsonian translocation 45, XX, -13, -14, t (13q/14q) pat.**

Introduction

Since genetic disease individually are quite unknown, it is rare that a practising obstetrician will encounter a patient with such a disease. They may influence pregnancy and this in turn influence the course of a number of genetic diseases. These effects may range from spontaneous abortion to chromosomal anomalies in liveborn children and in adults with certain types of faulty development. About 50 to 60% of all first trimester abortions are associated with derangement of one or more chromosomal complements (Holzgreve *et al* 1984). Abnormal chromosomal complement is more likely in first trimester miscarriages. There are about 30 to 35% chances of having another miscarriage in a couple having two or three miscarriages (Holzgreve *et al* 1984). In the present study chromosomal abnormalities in couples with more than two repetitive spontaneous abortions is reported.

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Material and Methods

Patients referred were subjected to clinical examination and the findings were recorded. The karyotype of all 14 couples having a minimum of two consecutive abortions were obtained from peripheral leukocyte cultures, processed according to the routine technique of Hungerford (1965). Flame dried slides were subjected to different staining techniques, such as, simple Giemsa staining, G-banding, C-banding and Q-banding. In each case at least a minimum of 30 metaphases were observed and atleast 5 plates were photographed and karyotyped as per the standard nomenclature for chromosome identification.

Plasma Progesterone was estimated in all patients by RIA, using Diagnostic Product Corporation (DPC) kit (coat-A-Count) (Kubasik *et al*, 1984), and ß-HCG by RIA, using Double antibody technique (Peterson and Swerdoff 1979).

Results

In these 14 cases, a total of 48 abortions were recorded. From these, 37 were of first trimester, 10 of second trimester, 1 of

TABLE I

Summary of 14 Cases With History of Spontaneous Abortion

Sr. No.	Age years wife	husband	Karyotype Wife	Husband	No. of spontaneous abortions 1st	2nd	3rd	stillbirth	P. Progesteron level in wife ng/ml
1.	28	32	46, XX	46, XY	—	2	—	1	10.5
2.	28	30	46, XX	46, XY	2	1	—	—	8.0
3.	26*	29	45, X/46, XX (20:80)a	46, XY	5	—	—	—	12.4
4.	38**	39	46, XX/46, XY (95:5)a	46, XY	7	—	—	—	9.0
5.	23	25	46, XX	46, XY	3	—	—	—	13.0
6.	27	28	46, XX	46, XY	1	1	—	—	16.1
7.	23	28	45, XX,—13,—14, t (13:14) pat	46, XY	3	1	—	—	10.0
8.	32	33	46, XX	46, XY	3	—	1	1	8.8
9.	30	34	46, XX	46, XY	2	—	—	2	9.6
10.	24	26	46, XX	46, XY	3	—	—	—	9.2
11.	24***	25	46, XX	46, XY	2	—	—	—	5.0
12.	29	30	46, XX	46, XY	3	4	—	—	13.0
13.	25	28	46, XX	46, XY	2	1	—	2	15.0
14.	22	24	46, XX	46, XY	2	—	—	—	14.5

Normal range for P. Progesterone: 8.0 to 18.0 ng/ml.

* : Normal having well developed secondary sexual characters. Later she conceived and delivered a healthy child.

** : Looking apparently normal with average height and weight. At the time of conception ß-HCG level was detectable every time but suddenly after 2-3 months ß-HCG level became negative suggesting arrest of further embryonic development. Further investigations were not possible as patient refused to come for followup. Fig. 1.

*** : Plasma Progesterone level is low.

a: Ratio of respective cell lines.

third trimester and 6 were stillbirths. The details are given in Table I.

As shown in Table I, three out of 14 couples were found to be cytogenetically abnormal.

Plasma Progesterone level on day 23rd of the cycle was normal in 13 patients. In one patient Progesterone level was 5.0 ng/ml on day 23rd of the cycle which is lower than the normal value.

Discussion

The incidence of chromosomal aberrations in couples with history of habitual multiple abortions varies from 3.2 to 32%. The most commonly observed chromosomal abnormalities include,

1. Aneupoidy (monosomy, trisomy) of autosomes or sex chromosomes. 2. Reciprocal translocations resulting in duplication or deletion of chromosome segments. 3. Balanced or unbalanced Robertsonian translocations and 4. Very rarely sex chromosome mosacism. Numerous reports of independent series have shown that balanced chromosomal rearrangements as well as aneuploidy (eg. chromosome 21 or monosomy (only Turner's)) in parents may predispose to recurrent fetal wastage (Byrd *et al*, 1977; De La Chapelle *et al*, 1973; Husslein *et al*, 1982; Khudr, 1974; Papp *et al*, 1974). In the present study one case showed mosaic cell line with 45,X/46,XX karyotype (20:80). Mothers with Turner's syndrome (or mosaic) normally do not achieve successful pregnancy, but when they do, spontaneous abortion, fetal anomalies or chromosome error occur in about 50% of conceptions (Dewhurst, 1978; King *et al*, 1978). Diedrich *et al* also reported an increased frequency (2.2%) of mosaicism for X-chromosome aneuploidy. Meiotic nondisjunction can explain the development of aneuploidy. Perhaps some factor in the internal milieu or external environment predisposes aneuploidy of X-chromosome.

In the present study we found one case of 13; 14 balanced translocation (Fig. 2). The frequency of balanced chromosomal translocations in live born infants has been estimated to be between 1 to 2 per 1000, which increases the risk of recurrence very substantially (McDonough and Tho, 1981). Robertsonian translocation, balanced or unbalanced is one of the most frequent structural chromosomal abnormalities found in the general population comprising half of all human translocations (Krishnamurthy *et al*, 1985). Such case may have a high risk of spontaneous fetal loss due to unbalanced chromosomal abnormality (monosomy, triploidy, aneuploidy trisomy).

It is known that corpus luteum deficiency is also responsible for recurrent fetal wastage; 23% and 35% of recurrent abortions in couples were reported (Tho *et al*, 1979; McDonough *et al*, 1981; Jones, 1975). The corpus luteum deficiency could be due to an inadequate ovarian production of progesterone. Out of the 14 cases studied for spontaneous abortion, borderline low level of plasma progesterone on day 23rd of the cycle was found in one case. Though we were not able to follow up this patient during pregnancy it is likely that corpus luteum insufficiency might cause spontaneous abortion. Folliculogenesis abnormality may be reflected in abnormal corpus luteum function, which is associated with pregnancy loss. Our findings suggest that not only chromosomal abnormality leads to spontaneous abortion but also an imbalance in the hormonal milieu soon after the LH surge might be one of the important factors causing re-

current abortions in mothers with normal chromosomes.

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See Figs. on Art Paper II