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CASE REPORT: ROBERTSONIAN TRANSLOCATION-ROB(13;14)(Q10;Q10) IDENTIFIED AS A POSSIBLE CAUSE OF RECURRENT MISCARRIAGES IN AN INDIAN COUPLE

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INTRODUCTION

• Couples with Recurrent Miscarriage (RM) have an increased risk of one of the partners carrying a structural chromosome abnormality, most commonly a balanced reciprocal or a Robertsonian translocation (ROB).

• Robertsonian translocation are special type of balanced translocation of the acrocentric chromosomes 13-15 and 21-22. The breakpoints mostly occur in the short arm, resulting in Dicentric chromosomes. E.g., rob(13;14), rob(14;21) being the most common ones.

•rob(13;14) has an incidence rate of 1/1000 live births. Carriers of a balanced translocation are usually phenotypically normal.

• Balanced carriers of Robertsonian translocation have an increased risk for infertility, miscarriages and chromosomally unbalanced offspring with multiple congenital abnormalities and intellectual impairment.

OBJECTIVE

To find and correlate the chromosome abnormality as the cause of recurrent abortion.

CASE PRESENTATION

An Indian couple (29Y/F & 35Y/M) with a clinical history of recurrent abortions (2.5 & 3.5 months) was referred for couple Karyotyping.

MATERIAL AND METHOD

A 72 hour peripheral blood lymphocyte culture was set up and processed further with standard protocols for karyotyping.

A total of twenty metaphases each were evaluated after GTG-banding at a 500-550 band resolution and reported according to International System for Human Cytogenetic Nomenclature (ISCN) 2016.

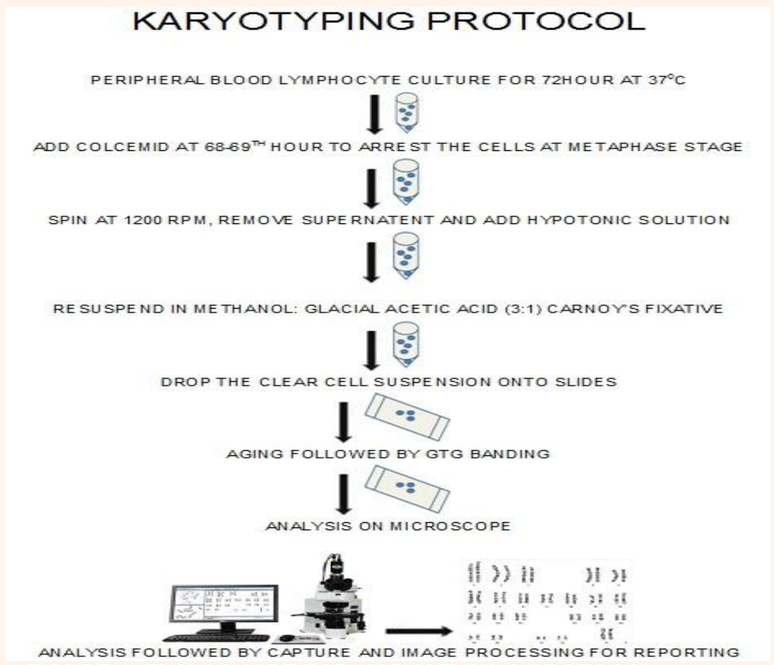

FIGURE 1: FLOW CHART FOR KARYOTYPING PROTOCOL

RESULTS

Chromosomal analysis of the couple revealed an abnormal karyotype in the wife with 45,XX,rob(13;14)(q10;q10) and a normal 46,XY in husband.

A balanced chromosomal rearrangement i.e. ROB involving both acrocentric chromosomes from D group i.e. chromosome 13 and 14 was identified. A balanced ROB is one of the most common cause of RM.

KARYOTYPE REPRESENTATION

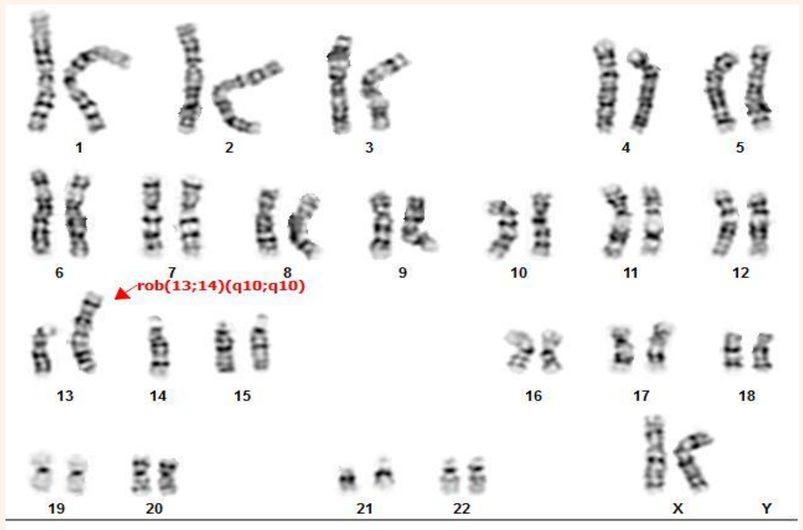

FIGURE 2: KARYOTYPE OF WIFE AS CARRIER OF ROBERTSONIAN TRANSLOCATION INVOLVING CHROMOSOMES 13 AND 14

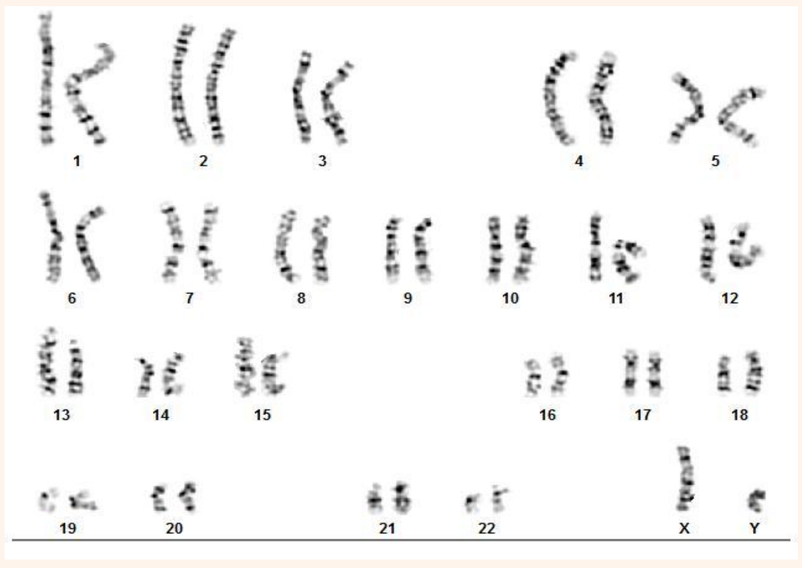

FIGURE 3: NORMAL KARYOTYPE OF HUSBAND

DISCUSSION

Peripheral blood Karyotyping of both partners should be performed in couples with recurrent miscarriage where testing of products of conception(POC) reports an unbalanced structural chromosomal abnormality.

As POC Karyotyping was not performed in this case, it becomes important to test the couple for any chromosomal anomalies.

One of the partner is a detected as carrier of Robertsonian translocation with chromosome 13 and 14.

The results of meiosis in a carrier of Robertsonian translocation illustrates that the chances of having a child with a normal karyotype would be low i.e. 1/6 and a carrier will be again, i.e., 1/6.

The two recurrent abortions in this case could be due to the outcome of unbalanced gametes resulting into Monosomy 13, Monosomy 14, Trisomy 13 – Patau syndrome and Trisomy 14.

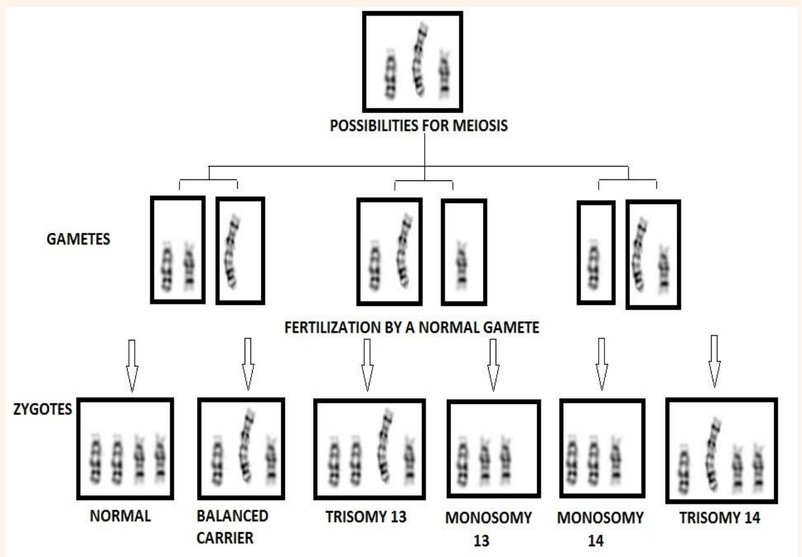

FIGURE 4: RESULTS OF MEIOSIS WITH ROBERTSONIAN TRANSLOCATION INVOLVING CHROMOSOMES 13 AND 14

DISCUSSION

Singh et al 2015, showed that the early detection of chromosomal aberration helps for appropriate genetic counselling and allows parents to make an informed reproductive decision on subsequent pregnancies. According to recent Royal college of obstetricians and Gynaecologists guidelines (2011), Cytogenetic analysis should be performed on products of conception of the third and subsequent consecutive miscarriages.

Couples whose carrier status was ascertained after two or more miscarriages have a low risk of viable offspring with unbalanced chromosomal abnormalities (Maureen T M Franssen et al 2006).

CONCLUSION

• The Robertsonian translocation rob(13;14) is identified as the possible cause of recurrent abortions in this case.

• It is emphasized that carriers of balanced translocation must be followed and directed to pre-implantation genetic diagnosis or preimplantation genetic screening to avoid fetal abnormalities.

• Cytogenetic analysis should be offered to all couples with unexplained recurrent abortions (Product of conception) to evaluate the probable presence of any chromosomal aberrations.

• Pre-implantation Genetic Diagnosis (PGD) has been proposed as a treatment option for translocation carriers.

FUTURE DIRECTIONS/PROPOSAL

Pre-implantation Genetic Screening or Pre-implantation Genetic Diagnosis (PGS/PGD)

• This is a special procedure in which embryos are evaluated for genetic abnormalities prior to being transferred into the uterus during In Vitro Fertilisation (IVF).

• This procedure is not offered at all fertility clinics because it is technically very difficult requiring experienced personnel.

• Pre-implantation genetic diagnosis has been used for couples who have been at risk for having offspring with single gene or X-linked disorders and in couples who themselves carry balanced chromosomal rearrangements.

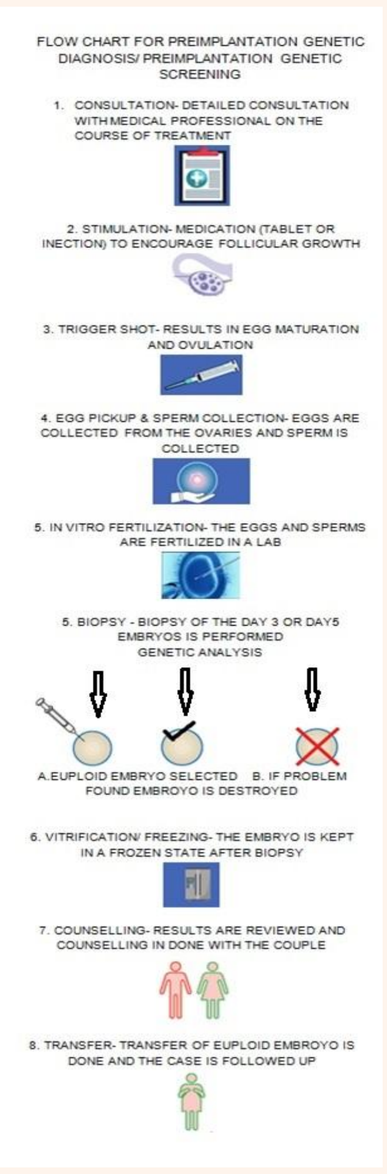

FIGURE 5: FLOW CHART FOR PRE-IMPLANTATION GENETIC SCREENING/ DIAGNOSIS (PGS/PGD)

ACKNOWLEDGEMENTS

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