Original Research Paper

Volume-8 | Issue-6 | June-2018 | PRINT ISSN No 2249-555X

Human Genetics

CYTOGENETICS AND GENETIC COUNSELING IN BAD OBSTETRIC HISTORY

Radhika Kedar — Department of Zoology, BMT and Human Genetics, School of Sciences, Gujarat University, Ahmedabad 380009, India

R J Verma — Department of Zoology, BMT and Human Genetics, School of Sciences, Gujarat University, Ahmedabad 380009, India

Dr.Divya Chandel* — Professor,Department of Zoology, BMT and Human Genetics, School of Sciences, Gujarat University, Navrangpura, Ahmedabad – 380009, India.*Corresponding author.

ABSTRACT About 15% to 20% of pregnancies end in spontaneous abortion (SA), mostly in the first trimester of which at least 50% result from chromosomal abnormalities. The TORCH (toxoplasmosis, rubella virus, cytomegalovirus and herpes simplex virus) infections are the most common infectious agents causing serious pregnancy outcome. The study aimed to perform karyotyping and genetic counseling in couples with bad obstetric history (BOH). A detailed proforma was filled for each case followed by peripheral blood lymphocyte cultures and G banding. In the Case 1, the wife had a reciprocal translocation with karyotype 46,XX,t(2;10)(q31;q25) and was also positive for TORCH test done previously. In the Case 2, the husband had a reciprocal translocation with karyotype 46,XY,t(q13;q32). Although in Case 1, the female was positive for TORCH test, this infection may be cause for single miscarriage but not a cause for repeated miscarriage. Therefore, karyotyping should be a mandatory etiological investigation followed by genetic counseling in all couples with BOH.

KEYWORDS : Chromosomal abnormality, Bad obstetric history, genetic counseling.

Introduction

Bad obstetric history (BOH) implies previous unfavourable fetal outcome including two or more consecutive spontaneous abortions, history of intrauterine fetal death, intrauterine growth retardation, stillbirth, early neonatal death, and/or congenital anomalies (Kumari et al., 2011). The causes could be multifactorial and are mostly associated with endocrine dysfunction, auto-immunity, infectious diseases, environmental toxins, congenital and structural uterine anomalies, chromosomal abnormalities etc. The most common reason for the first trimester miscarriage is a genetic defect in the embryo. The frequency of chromosomal anomalies among couples with recurrent miscarriage varies from 0.08% to 0.3% of normal population (Kochhar and Ghose., 2013). The abnormalities associated with recurrent pregnancy loss (RPL) include translocation, inversion, recurrent aneuploidy etc. The TORCH (toxoplasmosis, rubella virus, cytomegalovirus (CMV) and herpes simplex virus (HSV) infections are the most common infectious agents causing asymptomatic or mild infection and serious consequences in the fetus (Stegmann., 2002). Amongst all, the genetic factors causing BOH are difficult to study because the fetus is lost at an early stage of development and is therefore difficult to examine.

Subjects and Methods

Case-1

A couple (29 years old Male and 27 years old Female, 5 years of Marriage span) was referred at the Department of Zoology, Gujarat University, Ahmedabad to check for Chromosomal translocation. They reported an abnormal USG finding in prenatal testing and detection of increased Nuchal fold in colour Doppler at third trimester scan report which was followed by spontaneous abortion.

Case-2

A consanguineous couple (31 years old male and 27 years old female) was referred for chromosome analysis. During their 4 years of marriage span they had three first trimester fetal losses and fourth loss at 6 months pregnancy due to cessation of heart beat. Cytogenetic investigation had not been performed on the previous abortus materials.

Other than BOH in the couples of Case 1 and Case 2, the family history was normal. Consent was taken from the patients in both cases.

2 ml of heparinized blood was taken and standard PHA stimulated lymphocyte cultures were set up in duplicate for chromosomal analysis. After the slide preparation the chromosomes were subjected to the Giemsa-Trypsin-Giemsa (GTG) banding technique. For each individual thirty metaphases were karyotyped under a microscope and 100 cells counted to rule out mosaicism.

Results

In Case 1 cytogenetic analysis showed normal chromosome in the female (46,XX) while the karyotype of the male showed 46,XY,t(5;9)(q13;q32) (fig:1). In case 2 Male showed normal karyotype (46,XY) and the female showed translocation 46,XX,t(2;10)(q31;q25) (fig:2). The female tested positive for Torch report for Rubella virus and cytomegalovirus.

Figure 1: Partial karyotype and ideogram of chromosomes 5 and 9 showing a balanced reciprocal translocation involving breakpoints 5q13and 9q32.

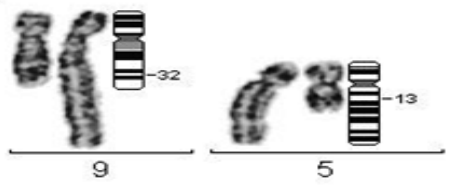
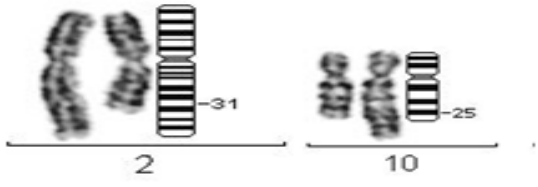


Figure 2: Partial karyotype and ideogram of chromosomes 2 and 10 showing a balanced reciprocal translocation involving breakpoints 2q31 and 10q25.



Couples who carry balanced reciprocal translocation have 50% chance of having spontaneous abortions and 20% risk of having children with abnormal genetic makeup because they can produce abnormal gametes during gametogenesis and transfer this abnormality to their fetus (Gardener et al., 2011). In both the present cases, one partner was carrying a balanced translocation. The carriers of a balanced reciprocal translocation are usually phenotypically normal because of a balanced complement of the genes. In addition to size of the chromosomal segment, the position and frequency of the break points also play a critical role because sometimes that region contains important genes

which may be responsible for development of embryo (Resim et al., 2013). In the first case, the male showed reciprocal translocation which is frequently associated with abnormal ultrasound findings in fetus and/or spontaneous abortion as observed in this case. In the second case the female showed the 46,XX,t(2;10)(q31;q25) karyotype and was positive for Torch test done previously. We conclude, that even if female is positive for TORCH, this particular infection may be cause for single miscarriage but not a cause for repeated miscarriage. Hence, cytogenetic analysis should be mandatory for all the couples with reproductive failures as also reported earlier (Chandel., 2016), and should be referred to a clinical geneticist. The carriers of such abnormalities should be informed about the risk of the birth defects. Those who carry balanced translocation should be given guidance concerning prenatal testing as these patients are at an increased risk of implantation failure and miscarriage. These cases highlight the importance of chromosomal analysis in such couples with BOH to rule out the possible genetic cause.

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