www.jmscr.igmpublication.org Impact Factor 3.79
ISSN (e)-2347-176x

IGM Publication Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Robertsonian Translocation – An Indication for Prenatal Diagnosis

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ABSTRACT
Robertsonian translocation occurs with a prevalence of 1 in 1000 in the general population. It carries reproductive risks that are dependent on the chromosomes involved and the sex of the carrier. Here we describe two families referred to our Genetic Division for karyotyping. Chromosomal analysis was done from peripheral blood lymphocyte culture. In case I index case was referred with complaint of primary amenorrhoea. Her Karyotype revealed 45XX t (13;14), inv(9). When parents karyotype was done, mother's karyotype revealed 46XX and father showed 45XY,t(13;14),inv(9). family had a baby, clinically diagnosed as having Down syndrome, died at 6 months of age. Karyotype of Mother revealed 45XX,t(14;21) and father had normal male chromosomal complement. In Robertsonian translocation careful risk assessment and proper genetic counselling is the most important thing.
Keywords- *Carrier, chromosomal aberrations, translocation, prenatal diagnosis, karyotype*

INTRODUCTION

Robertsonian translocation is an unusual type of chromosomal rearrangement, which involves two acrocentric chromosomes that fuse near the centromere region with loss of the short arms. Because the short arms of all five pairs of acrocentric chromosomes have multiple copies of genes for ribosomal RNA, loss of the short arms of two acrocentic chromosomes is not deleterious [1]. It

occurs with a prevalence of 1 in 1000 in the general population [2].

The most common are the nonhomologus forms i.e. those involving two different acrocentric chromosomes, either two different D group chromosomes (chromosomes 13, 14 and 15), two different G group chromosomes (21 and 22), or a D group and G group chromosome [2]. Although Robertsonian translocations involving all combinations of the acrocentric chromosomes have been detected, two (13q14q and 14q21q) are relatively common [1]. It has been found that the P arms of chromosome 13 and 14 have similar sequences arranged in an inverse manner. This makes them pair during meiosis and prone to recombination. The most common Robertsonian translocation is between chromosomes 13 and 14. This D/D translocation makes up 75% of all Robertsonians. The potential live born chromosomally unbalanced outcome of this is translocation trisomy 13 (Patau syndrome).There is also potential for uniparental disomy for chromosome 14 following trisomy rescue with an estimated risk of 0.1 – 0.5%.Translocation trisomy 14 is expected to result in first trimester loss. Some individuals with t (13;14) present with infertility or recurrent spontaneous abortions [2],[4]

The most common Robertsonian after the t (13;14) is the t (14;21). The potential liveborn unbalanced outcome of this D/G Robertsonian is translocation trisomy 21resulting in Down syndrome [2],[4].

When the translocation is balanced, the person with it is called a Robertsonian translocation carrier. As carriers are healthy and have a normal lifespan, many never discover about their unusual chromosome rearrangement. Although a carrier of a Robertsonian translocation is phenotypically normal, there is a risk of unbalanced gametes and therefore of unbalanced offspring. In fact, the translocation can be passed down in families for many generations without anyone discovering it. An unbalanced Robertsonian translocation may come to light after a baby is born with a chromosomal aberration [3].

Prenatal diagnostic techniques are used to diagnose foetal genetic disorders in utero and it has been proved an important milestone in medical genetics and has so altered the outlook for families at risk of having affected children [3].

CASE REPORT

Here we report two cases of Robertsonian translocation. In both cases; chromosomal preparation was obtained from peripheral blood leucocyte culture using standard procedures. Chromosomal preparations were subjected to GTG – banding and karyotyped using ISCN classification.

Case I

Index case was a 16 yr old female patient, referred for karyotyping with the chief complaints of primary amenorrhoea and short stature. Analysis of family history and pedigree charting revealed II^{o} consanguinity. Antenatal and postnatal history was uneventful.

On clinical examination, patient was short with the height of 123 cm (< third centile). Secondary sexual characteristics were not well developed. Genital

system examination showed ambiguous genitalia with cliteromegaly and vaginal orifice was absent.

Hormonal profile showed increased levels of Serum LH and Serum FSH i.e 11.25miu/ml and 89.14 miu/ml respectively.

Ultrasonographic study revealed small infantile uterus 2.1 X 1.4 X 0.6 cms and streak bilateral gonads.

Cytogenetic analysis of this patient revealed a balanced translocation, 45XX, t(13;14), inv(9).On revealing that the patient is Robertsonian translocation carrier, parents of patient were called for karyotyping. Mothers karyotype revealed 46XX chromosomal complement .Her father showed 45 XY,t(13;14), inv (9), a balanced Robertsonian translocation.

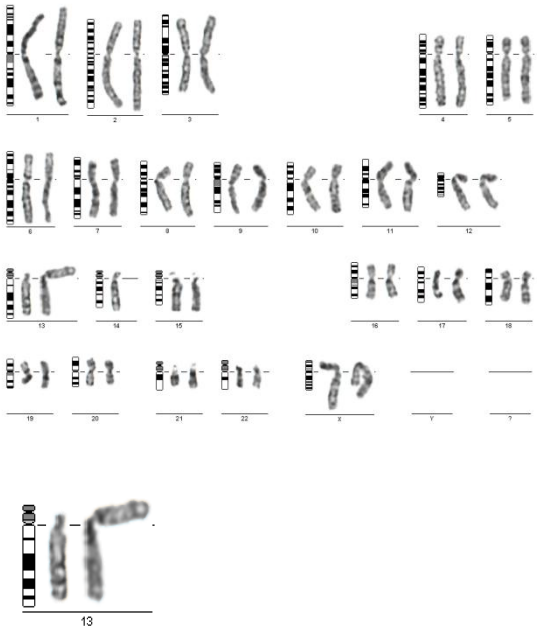

Figure 1: Karyotype, 45XX,t(13;14),inv(9)

Case II

An apparently healthy couple, married for 2 years was referred for Karyotyping and subsequent genetic counseling. Age of the female spouse was 22 years and age of male spouse was 26 years. History revealed that they had given birth to a female child with birth weight of 4 kilograms, baby cried immediately after birth. Antenatal history was uneventful. The child soon started losing weight and had delayed milestones. Subsequently this child died at the age of 6 months.

Analysis of family history and pedigree charting revealed, non consanguineous marriage. No history of mental retardation in the family members.

On Investigations, echocardiography of child revealed AV cushion defect, ASD, VSD with right to left shunt.

Cytogenetic analysis of this child revealed 46, XX, t (14;21) chromosomal complement. Cytogenetic analysis of mother revealed 45XX, t(14;21) chromosomal complement while father had normal 46, XY chromosomal complement.

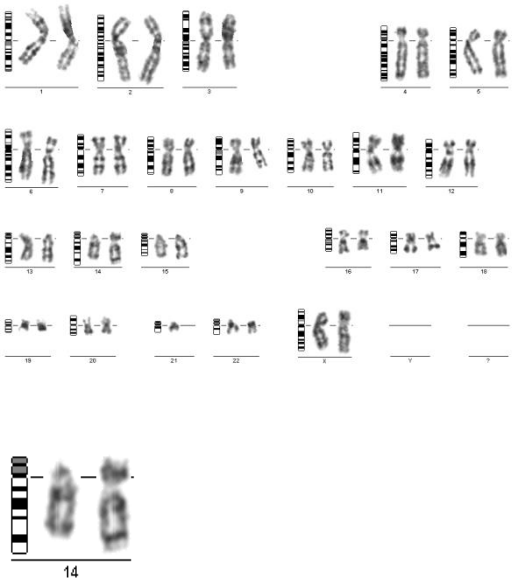

Figure 2: Karyotype ,45,XX, t(14;21)

DISCUSSION

Case I

Chromosome aberration such as t(13;14) in combination with inv (9) is a very rare finding in patient with primary amenorrhoea. The father's chromosomal analysis showed t (13; 14), inv (9) and found to be carrier. The direct phenotypic effect of t(13;14) was not expressed in proband as well as in her father.

The inversion (9) is one of the most common balanced structural chromosomal aberrtions and has been considered to be a normal variant rather than an abnormal karyotype. However review of literature showed its association with infertility, recurrent abortions, schizophrenia and other abnormal clinical conditions as well as chromosomal abnormalities arising as a result of having inv (9). Inversion (9) is the most frequent finding in females with primary amenorrhoea and testicular feminization [5].

As proband had primary amenorrhoea and short stature, estrogen – progesterone replacement therapy will help her to gain height, develop secondary sexual charecteristics and to achieve menstrual cycles. Referral for vaginoplasty and breast reconstruction surgery if desired.

The risk of inheritance was 1.6 to 3.4% for Robertsonian transloction and for inversion 9 it was 5 to 10% as father was affected.

In case II, the affected child had chromosomal complement 46, XX, t (14/21), which is translocation Down syndrome. The incidence of translocation Down syndrome is 4%. The genetic risks in such situation depend entirely on whether there is an abnormality in the parental chromosomes [3]. Her mother had a balanced Robertsonian translocation, in which chromosomal number was 45, including the translocation chromosome, which is made up of the long arms of two chromosomes (q14 q21) so the total amount of chromosomal material was normal [1].

If one of the spouse is balanced translocation carrier and other spouse is normal possibilities for offspring in families with translocation Down syndrome is 10%. In fact this risk is less, particularly when father is carrying the balanced translocation. If a women is already having a Down syndrome baby the risk is higher for subsequent pregnancies i.e. 1 in 8 pregnancies.[3]

CONCLUSION

Both cases had strong indication for prenatal diagnosis for future pregnancy and it was well explained to patients and their parents. Other relatives should also be offered testing in order to identify unsuspected balanced translocation carriers (of either sex), who can then be offered prenatal diagnosis in any future pregnancy. In both these cases genetic counselling plays a crucial role.

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