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CASE REPORT

Recurrent Abortions and Down Syndrome Resulting from Robertsonian Translocation 21q; 21q

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Aim: The purpose of the present research was a presentation of case report of Robertsonian translocation composed of homologous chromosomes 21q;21q and reproductive risk found in the family affected by this type of translocation. **Methods:** Cytogenetic diagnosis has been done on chromosome preparations of lymphocytes cultured from peripheral blood by Moorhead method. **Results:** Analyses of cytogenetic diagnosis was performed on the couple who has been through 10 spontaneous miscarriages and two additional births with Down syndrome. The woman had Robertsonian translocation between homologous chromosomes 21: 45XX,der(21;21)(q10;q10), and there was no change in her phenotype, whereas her husband had a normal phenotype and karyotype: 46, XY. Their first child with Down syndrome symptoms did not undergo the cytogenetic analysis. By cytogenetic analysis it was discovered that their second child has Trisomy 21 with Robertsonian translocations between homologous chromosomes 21: 46,XY,+21,der(21;21)(q10;q10)mat, and that he inherited it from his mother. **Conclusion:** Chromosomal aberration that our patient suffered from and that is presented in this paper has caused spontaneous miscarriages and birth of children with Down syndrome. Based on cytogenetic analysis in prenatal diagnosis and genetic consultation of affected family with Robertsonian translocation 21q;21q, it is unlikely to select healthy offspring by a parent with that aberration. Key words: Robertsonian translocation, Down syndrome, recurrent abortions.

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1. INTRODUCTION

Robertsonian translocations are recognized to be the most common structural chromosomal aberrations in the population with an incidence of 1.23/1000 live births (1). Among the couples with a large number of spontaneous miscarriages, one of the spouses can be silent carrier of Robertsonian translocation (2). Robertsonian translocation is created by fusion of two acrocentric chromosomes at or near the centromere; as a result two chromosomal long arms are joined together, thus creating a single chromosome, while their short arms which contain a small amount of genetic material are lost. The missing genetic material contains only ribosomal genes. Since ribosomal genes are present also in short arms of other acrocentric chromosomes, lost genetic material of these persons will not cause changes in phenotype. Robertsonian translocation can arise between different acrocentric chromosomes. In many papers published by various authors it is reported that Robertsonian translocations most often occur between the acrocentric chromosomes 13 and 14 (3). The pathogenesis of Robertsonian translocations occurs during meiosis, and to these persons is created gametes in deficit or surplus of genetic material. For these reason silent carriers of Robertsonian translocations have higher risk of spontaneous miscarriages and born children with anomalies. The level of this risk depends on the gender of the carrier and the type of Robertsonian translocation. Carriers of Robertsonian translocations created by unhomologous chromosomes have the opportunity to pro-

duce unbalanced, balanced and normal gametes (4). The risk level of this type of translocation depends on the gender of translocation carrier.

Robertsonian translocations formed by homologous acrocentric chromosomes cause higher risk in reproductive ability of the carrier (5). With this type of translocation, carriers of both sexes possess the maximum risk for spontaneous miscarriages or birth of children with anomaly. Carriers of the Robertsonian translocations created between homologous chromosomes 21q;21q are at a high risk of giving birth to malformed children with the Down syndrome and spontaneous miscarriages (6). In families affected by this type of translocation, early cytogenetic diagnosis and genetic counseling enable prevention of giving birth to child affected with Down syndrome and spontaneous miscarriages. In our case when the carrier of this translocation was not detected in time through cytogenetic diagnosis, but it was discovered later after birth, to observe the consequences of Robertsonian translocation 21q;21q, we were determined to show the real reproductive condition of the family that owns this translocation type.

2. AIM

The purpose of this study was to analyze chromosomes of a family affected by homologues Robertsonian translocation for 21q;21q, and through it to determine reproductive risk and explain etiological factor of giving birth to two children with Down's syndrome and 10 spontaneous miscarriages.

3. METHODS

Cytogenetic diagnosis has been done in chromosome preparations of lymphocytes cultured from peripheral blood according to Moorhead method (7). For precise identification of chromosomes standard method for G-banding by Seabright was used (8).

4. CASE PRESENTATION

The patient (MR), born in 1974, was referred to Obstetrics Gynaecology Clinic in Prishtina for examination in order to detect the cause of the birth of children with Down syndrome and recurrent miscarriages. The patient has had 12 pregnancies, 10 of which ended with spontaneous abortions, mostly in the first trimester of pregnancy (Figure 1. II_2-II_{11}). Chromosomal analyses were not performed for any of the recurrent spontaneous miscarriages. The first and the last pregnancies have ended with suspected children birth with Down syndrome (Figure 1. II_1 and II_{12}). The first female child, who had congenital heart defects, has lived 12 days. Even though there were typical clinical symptoms of Down syndrome, but due to the war in Kosova and because of her early death the karyotype of that child was not performed. The cytogenetical analysis was done on the second child with the clinical symptoms characteristic for Down syndrome and the existence of male karyotype of the Robertsonian translocation between homologous chromosomes 21: 46,XY,+21,der(21;21)(q10;q10) (Fig. 2). To prove that child's chromosomal aberration occurred de novo or it was inherited from parents were made cytogenetical analysis of child's parents. Karyotype of the father was normal (46, XY), while the Robertsonian translocation between homologous chromosomes 21: 45, XX, der (21;21)(q10:q10) was detected in the mother karyotype (Figure 3). The mother karyotype confirmed that the child's translocation had not occurred *de novo* but it was inherited from mother side. Parents of affected mother had normal karyotype, thus Robertsonian translocation of the mother was *de novo* created through fusion of long arm of homologous chromosomes 21q;21q near to their centromere region (Figure 4).

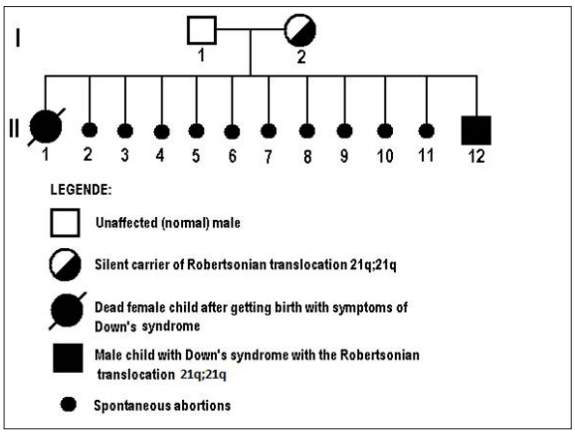

Figure 1. Pedigree of the affected family with the Robertsonian translocation 21q;21q.

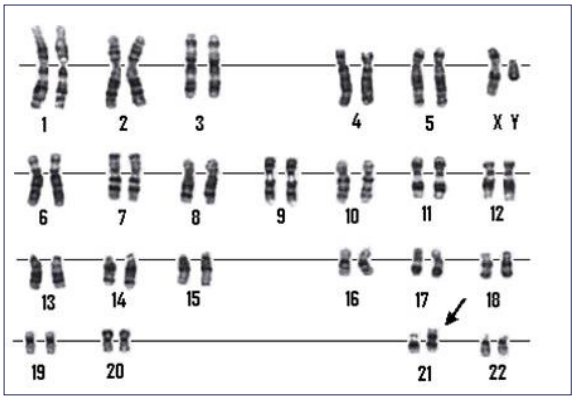

Figure 2. The child karyotype with the Robertsonian translocation of 46, XY, +21, der (21; 21) (q10: q10) mat.

5. DISCUSSION

The Robertsonian translocation between homologous chromosomes 21q;21q presented in the above case is one of the very rare chromosomal abnormalities found in the general population. Carrier of this type of translocation faces a higher risk of reproductive complications. Reproductive state of the presented case shows all possible effects of the Robertsonian translocation 21q;21q in carrier reproductive performance, and in this respect our results are consistent with the results of the cases presented by other authors (6). Many authors studies by using a FISH method have proven that the Robertson translocation 21q;21q carrier can only produce gametes that are disomic for chromosome 21 or nullisomic for chromosome 21 (9, 10). The union of these gametes with normal gametes of the other partner can create offspring with monosomy or trisomy 21 with translocation 21q;21q. Since she can create only babies with monosomy 21 or trisomy 21, the presented patient with translocation 21q;21q had a high reproductive risk. Monosomy 21 was a cause of pregnancy loss and recurrent miscarriages' of the carrier patient. Trisomy 21 with translocation may be the cause of the birth of children with

Down's syndrome or intrauterine fetal death ending in spontaneous miscarriages. Carrier of this translocation cannot make normal or balanced gametes; she has not given birth to a normal child. Compared to Robertsonian translocation created by fusion of nonhomologous acrocentric chromosomes where the risk level depends on carrier gender, the carriers of the Robertsonian translocation 21q;21q have 100% risk for giving birth to children with the Down syndrome and for recurrent miscarriages regardless of sex (5). This is confirmed by the patient's reproductive actual state presented in this paper who had no healthy child born alive, but has 2 children with Down's syndrome (Figure 1. II_1 and II_{12}) and 10 other spontaneous miscarriages (Figure 1. II_2-II_{11}).

For these families, cytogenetics early diagnosis and genetic counseling are very important for the prevention of birth of children with Down syndrome and spontaneous miscarriages. If through cytogenetics diagnosis of the mother and her first Down's syndrome child were revealed Robertsonian translocation 21q;21q (Figure 1. I_2 and II_1) the high reproductive risk consequences would be decreased and thus giving birth to children with Down syndrome and 10 spontaneous miscarriages would be prevented that had had a highly negative effect on the health condition, psychological status and welfare of the affected family.

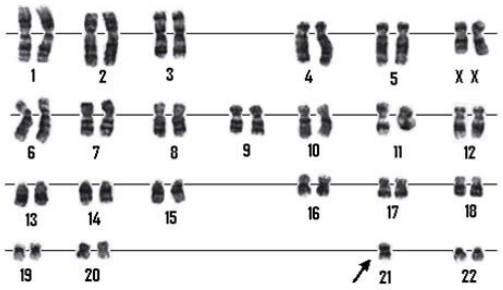

Figure 3. The carrier maternal karyotype of the Robertsonian translocation 45, XY, +21, der (21; 21) (q10: q10).

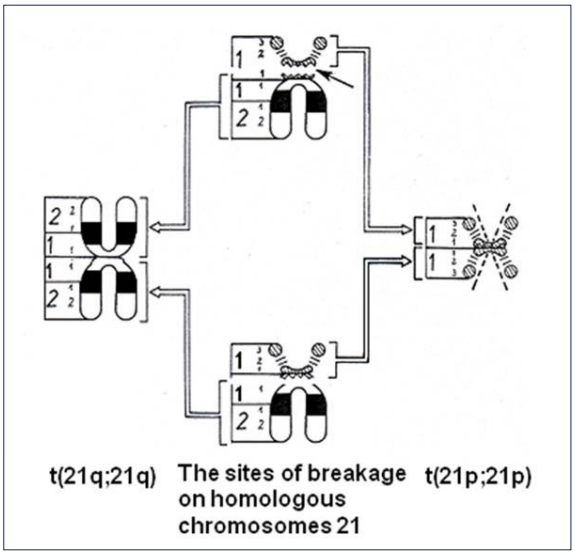

Figure 4. Schematic representation showing the creation of the Robertsonian translocation between homologous chromosomes 21q;21q.

6. CONCLUSION

The conclusions of the cytogenetic studies are as follows:

Affected family by this type of translocation possesses a high risk (100%) to spontaneous miscarriages and giving birth to children with Down syndrome.

The most common cause of early recurrent abortions is monosomy of chromosome 21, as a result of fusion of nullisomic gametes which have no normal chromosome 21, with the partner's gametes.

In this family the children born with Down syndrome are result of the fusion of carrier's disomic gametes that have possessed the Robertson translocation 21q, 21q with normal gametes of the other partner.

Since it's impossible to make euploid gametes with normal or balanced chromosomes, the carrier affected by the Robertsonian translocation 21q;21q is unable to give birth to normal children which are phenotypically and genetically normal. Couples may decide not to have children.

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