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Original Article

Chromosomal translocations detected by prenatal and postnatal genetic diagnosis: our experience

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Abstract: Objective: The aim of this study was to compare the frequency of chromosomal translocations in postnatal and prenatal cases in a single laboratory in China, and to investigate the rates and indications of chromosomal translocations in postnatal diagnosis and prenatal diagnosis. Study design: 17,991 postnatal cases with reproductive failure or congenital anomalies and 4198 prenatal cases with indications for amniocentesis in Northeast China were enrolled. Chromosomal karyotype analysis was performed on blood samples and amniotic fluid samples with standard G-banding. In prenatal cases found to have chromosomal translocations, the couples were recalled for performing karyotype analysis to analyze the origin of chromosomal translocations. Results: The frequency of chromosomal translocations in postnatal cases (1.26%, 227/17991) was statistically significant difference as compared with prenatal cases (0.64%, 27/4198). According to the reasons for postnatal diagnosis, the highest incidence of chromosomal translocations was found in cases with congenital anomalies (2.04%), followed by recurrent miscarriages (1.75%), infertility (1.06%) and previous abnormal offspring (0.74%). For prenatal diagnosis, the highest incidence of translocations was found in cases with the indication of parent with abnormal karyotype (27.72%), followed by previous abnormal child (3.12%), abnormal ultrasound findings (1.46%), advanced maternal age (0.47%), biochemical abnormal screening (0.42%). There were 12 cases of unbalanced translocations detected in postnatal cases and 4 cases in prenatal cases. Conclusion: The incidences of chromosomal translocation in patients with different indication make a big difference. The reason for ascertainment of the translocation should be taken into account when counseling these patients.

Keywords: Reciprocal translocation, Robertsonian translocation, prenatal diagnosis, postnatal diagnosis, genetic counseling

Introduction

Translocations are chromosomal abnormalities that occur when chromosomes break and the fragments rejoin other chromosomes. It can further be classified into balanced and unbalanced rearrangements. When two nonhomologous chromosomes break and exchange fragments, new chromosomes, called derivative chromosomes, are formed. Taking into account data reported in several studies of newborns, which include 59,514 cases, translocations are the most frequent structural aberration in humans with an incidence of 0.178%, 0.092% corresponding to reciprocal translocations and 0.086% to Robertsonian translocations [1]. Most balanced translocation carriers are phenotypically normal because there is no loss or gain of genetic information [2, 3]. However the production of gametes with unbalanced segregation during meiosis of the chromosome involved in the translocation can be associated with reproductive failures, such as recurrent spontaneous abortions or stillbirth, infertility, and malformed childbearing history [4]. Thus in couples experiencing repeated pregnancy losses, the incidence of chromosomal translocations (1.88%, and 0.81% corresponding to reciprocal and Robertsonian translocations, respectively) is higher than the incidence present in newborn series [5]. Summarizing the data, female translocation carriers (65.7%) are about twice as frequent as male translocation carriers (34.3%) among these affected couples. Unbalanced translocations with a lack or excess of genetic material often result to miscar-

Table 1. Number of patients according to different indications

Chromosome analysis indication	Case Number		
	Male	Female	Total
Postnatal diagnosis	10066	7925	17991
Infertility	6764	4954	11718
Miscarriages or stillbirth	2223	2223	4446
Congenital anomalies	575	308	883
Previous abnormal offspring	472	472	944
Prenatal diagnosis	-	-	4198
Advanced maternal age	-	-	856
Abnormal ultrasound findings	-	-	137
Biochemical abnormal screening	-	-	3078
Parent with abnormal karyotype	-	-	18
Previous abnormal child	-	-	96
Others	-	-	13

riages or offspring with mental and/or physical disability. It may be inherited from a parent who carries the balanced form of the rearrangement or arise *de novo*.

Recurrent translocations may be mediated by nonallelic homologous recombination (NAHR) between segmental duplications or paralogous interspersed repeats [6, 7]. Palindromic AT-rich repeats on Chromosomes 3, 8, 11, 17, and 22 also generate recurrent translocations, the most common of which is the recurrent t(11;22) that causes Emanuel syndrome [8]. ROBs in the general population is nonrandom, with der(13q14q) and der(14q21q) constituting up to 85% of all ROBs and all other types of ROBs constituting the remaining ~15% of these translocations. It was proposed that the high prevalence of ROBs is because of the similarities of the DNA sequences shared by the short arms of acrocentric chromosomes which confer susceptibility to chromosome rearrangement [9].

Chromosomal translocations are considered to be one of the most important causes of the reproductive failure, even the unbalanced translocations lead to monosomy and trisomy for segments of different chromosomes and account for ~1% of cases of developmental delay and intellectual disability. It is invaluable in many ways to know the prevalence of both balanced and unbalanced chromosomal translocations in Chinese populations. In the current study, we shared our large collection of chromosomal translocations identified postnatally and prenatally in a single laboratory in China.

Materials and methods

From August, 2010 to April, 2015, we successfully performed karyotype analyses for 17,991 human postnatal specimens (10,066 males and 7925 females) and 4198 prenatal specimens (amniotic fluids) in the laboratory of the Center for Reproductive Medicine and Prenatal Diagnosis, The First Hospital of Jilin University, Changchun, Jilin province, China. Referral reasons for postnatal diagnosis were infertility, recurrent spontaneous abortions, congenital anomalies, and previous abnormal offspring. The reasons for prenatal diagnosis were advanced maternal age, abnormal ultrasound findings, a parent with abnormal karyotype, abnormal biochemical markers in maternal serum, previous history of a fetus/child with chromosomal abnormalities or congenital anomalies and others that including a family history of chromosomal abnormalities and noninvasive prenatal testing (NIPT) positive (**Table 1**). Appropriate written voluntary consent was obtained from all the individuals and the study was approved by the Medical Ethics Committee of First Hospital of Jilin University.

Karyotype analysis of 17991 postnatal diagnosis patients was performed. Briefly, peripheral blood lymphocytes were cultured in lymphocyte culture medium (Yishengjun; BaiDi Bio-Technology, Guangzhou, China) at 37°C for 72 h, followed with 50 μg/ml colchicine (Yishengjun; BaiDi Bio-Technology, Guangzhou, China) arrest of mitosis for 1 h before culture termination. Amniocentesis was performed between 16 and 18 weeks of gestation, when the procedure is safest. Under ultrasonographic guidance, the insertion angle and direction of the needle was determined at the best point where fluent amniotic fluid and limbs of the fetus were observed, avoiding the placenta and umbilical cord, 25 milliliter of amniotic fluid was collected (the first 1-2 ml of amniotic fluid was discarded) and transferred directly to the laboratory for culture. After centrifuged at 1500 r/min for 6 minutes, discarding the supernatant, 1~1.5 ml of cell suspension was inoculated in 5 ml of culture media (GBICO AmnioMAX-II complete, USA), cultured for 6-7 days at 37°C and 5% CO_2 until cell growth was observed under an inverted microscope. G-banding (350-400 bands level) was performed for chromo-

Table 2. Frequency of translocation according to different indications

Indication	N (%)		
	Male carriers	Female carriers	Total
Postnatal diagnosis	131 (1.30)	96 (1.22)	227 (1.26)
Infertility	89 (1.32)	35 (0.71)	124 (1.06)
Recurrent miscarriages	31 (1.39)	47 (2.11)	78 (1.75)
Congenital anomalies	7 (1.22)	11 (3.57)	18 (2.04)
Previous abnormal offspring	4 (0.85)	3 (0.64)	7 (0.74)
Prenatal diagnosis			27 (0.64)
Advanced maternal age			4 (0.47)
Abnormal ultrasound findings			2 (1.46)
Biochemical abnormal screening			13 (0.42)
Parent with abnormal karyotype			5 (27.78)
Previous abnormal child			3 (3.12)
Others			0 (0)

somal sample preparation, Twenty metaphases were microscopically analyzed for non-mosaic cells and fifty metaphases were analyzed for mosaic cells, and chromosomal translocations were reported according to the International System for Human Cytogenetic Nomenclature [10].

Statistical analysis was performed with SPSS® version 17.0 statistical package (SPSS Inc., Chicago, IL, USA) for Windows®. The Chi-square test and Fisher's exact test was used to compare statistical significance between chromosomal translocations of the prenatal cases and postnatal cases. A *P*-value >0.05 was considered to be no statistically significant and all *P*-values were two-sided.

Results

In the 17,991 postnatal diagnosis cases with adverse reproductive outcome or congenital anomalies, there were 227 patients with chromosomal translocations, including 131 male carriers and 96 female carriers. The incidence of total variants in the postnatal diagnosis individuals was 1.26% (227/17,991). There was a significant difference as compared with prenatal diagnosis cases 0.64% (27/4198) (*P*= 0.0007). According to the reasons for postnatal diagnosis, the highest incidence of chromosomal translocations was found in cases with congenital anomalies (2.04%), followed recurrent miscarriages (1.75%), infertility (1.06%) and previous abnormal offspring (0.74%). In the cases with infertility, the male carriers was significant more than the females (*P*=0.0015). Otherwise the female carriers were significant more than the males in the cases with congenital anomalies. In the other cases, there was no significant difference between the male carriers and females. The total incidence of chromosomal translocations was 0.64% in the prenatal diagnosis cases. The highest incidence of translocations was found in cases with the indication of parent with abnormal karyotype (27.72%), followed by previous abnormal child (3.12%), abnormal ultrasound findings (1.46%), advanced maternal age (0.47%), biochemical abnormal screening (0.42%). And in other indications, there was no translocation (**Table 2**).

In postnatal diagnosis cases, the involving chromosome number of balanced translocation between two chromosomes was shown in **Table 3**. The horizontal rows were the first translocated chromosome numbers, and the vertical rows were the second translocated chromosome numbers. In the cases with reproductive failure, the Robertsonian translocations with der(13;14) was the most common variant (n=32), and the der(14;21) was the second (n=10). In the cases with congenital anomalies, the balanced translocations were t(1;6), t(2;9), t(2;14), t(4;5), t(7;9), t(13;14), t(X;5), t(X;22). However, the breakpoints occuring on the same chromosome were different. Excepted for the Robertsonian translocations, the localization of breakpoints occurred more frequently on chromosome 1, 3, 4, 11 (the frequency more than 20 times).

The karyotypes of 21 patients of mosaic/complex/unbalanced translocations and their clinical manifestations were showed in **Table 4**. There were 2 mosaic balanced translocations including one being both mosaic and complex (Case 1 with concurrent existence of inv(8) and t(18;20) in one cell population and a t(18;20) in the other cell population) and one with a mosa-

Table 3. Total Cases of balanced translocations detected in postnatal cases of this study

Chromosome No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	X	Y	T
1		4	3	2		1[Δ]	1		1	2	4	3	4	2		1		1	1	1	1				32
2				1		1		1	1.1[Δ]		1		2	1.1[Δ]	1	1						1			13
3					2	3	3		2		1	2			2		1			2		1			19
4					1[Δ]	3			1	2	4	2		1		1	1			1		1			18
5													2		2			5		1	1	1			12
6							1	1		1		2		1				1	1	1					9
7								1	1[Δ]	2			1	1	2			1							9
8									1		1			1											3
9											1				1				1						3
10															2		1	1	1			1			6
11													1	1			1					4			7
12														1					1						2
13														31.2[Δ]	2		1		1		3				40
14																				1	10	3			14
15																	1	1			2				4
16																									0
17																		1	1			1			3
18																				1					1
19																						1			1
20																									0
21																						2			2
22																									0
X		1	1		1[Δ]					1	1								1			1[Δ]			7
Y																1									1
T		5	4	3	4	8	5	3	8	8	13	9	10	43	12	4	6	11	8	8	17	17	0	0	206

[Δ]represent indication of Congenital anomalies.

Table 4. Total cases of mosaic/complex/unbalanced translocations detected in postnatal cases of this study

Case	Sex	Age	Karyotype	Reason for referral
1	M	30	46,XY,inv(8)(p21q24),t(18;20)(q21;p11)[21]/46,XY,t(18;20)(q21;p11)[29]	Idiopathic infertility
2	M	35	46,XY,t(11;17)(q11;p13)[7]/46,XY[93]	Recurrent miscarriages
3	F	27	46,XX,?t(1;5;20)(q42;q13;p11.2)	Idiopathic infertility
4	F	27	46,XX,t(2;4;10)(q37;q31;q22)	Recurrent miscarriages
5	M	24	46,XY,t(3;18;17)(q27;q21;q21)	Idiopathic infertility
6	M	36	46,XY,t(6;7)(q13;p15),inv(9)(p11;q13)	Idiopathic infertility
7	M	34	45,XY,t(1;11)(q25;q23),rob(15;22)(q10;q10)	Idiopathic infertility
8	F	21	45,XX,-17,der(17)t(17;22)(p13;q11.2),-22	Idiopathic infertility
9	M	24	45,XY,der(10)t(10;15)(q26;q11.2),-15	Azoospermia
10	M	28	46,X,?der(Y;Y)(q10;q10)	Idiopathic infertility
11	M	37	45,XY,-13,-19,+der(19)t(13;19)(q12;p13)	Oligospermia
12	M	24	45,X,der(Y;22)(q10;q10)	Oligospermia
13	F	39 day	46,XX,der(11)t(2;11)(q33;q23)	Congenital anomalies
14	F	5	47,XX,t(5;20)(q13;q12),+21	Suspicion of Down syndrome
15	M	4 day	46,XX,der(14;21)(q10;q10),+21	Suspicion of Down syndrome
16	F	19 day	46,XX,der(14;21)(q10;q10),+21	Suspicion of Down syndrome
17	F	1	46,XX,der(14;21)(q10;q10),+21	Suspicion of Down syndrome
18	F	30	47,XX,t(17;22)(q21;q11),+21	Intellectual disability and pregnant
19	M	36 day	46,XY,der(21;21)(q10;q10),+21	Suspicion of Down syndrome
20	M	5	46,XY,der(21;21)(q10;q10),+21	Suspicion of Down syndrome
21	M	7 day	46,XY,+21,der(21;22)(q10;q10)	Suspicion of Down syndrome

Table 5. Total cases of balanced/unbalanced/complex translocations detected in the prenatal cases of this study

Case No.	Maternal age	Gestational age	Fetus karyotype	Indications for prenatal genetic diagnosis	Parental karyotype
1	27	17w+	45,XN,der(14;21)(q10;q10)	History of a child with Down syndrome	
2	27	17w+	45,XN,der(21;22)(q10;q10)	Parent with abnormal karyotype	45,XX,der(21;22)(q10;q10)
3	31	18w+	45,XN,der(13;14)(q10;q10)	Parent with abnormal karyotype	45,XX,der(13;14)(q10;q10)
4	25	19w+	45,XN,der(13;21)(q10;q10)	Biochemical abnormal screening	
5	36	18w+	45,XN,der(13;14)(q10;q10)	Advanced maternal age	45,XY,der(13;14)(q10;q10)
6	24	19w+	46,XN,t(1;13)(p22;q32)	Parent with abnormal karyotype	
7	32	19w+	46,XN,t(1;22)(p22;q11)	Biochemical abnormal screening	46,XY,t(1;22)(p22;q11)
8	27	18w+	46,XN,t(2;10)(q11;q11)	Biochemical abnormal screening	
9	31	18w+	46,XN,t(3;9)(q21;q22)	Biochemical abnormal screening	46,XY,t(3;9)(q21;q22)
10	34	19w+	46,XN,t(3;19)(q12;q13)	Biochemical abnormal screening	46,XY,t(3;19)(q12;q13)
11	34	19w+	46,XN,t(4;14)(q13;q11)	Ultrasound markers	46,XX,t(4;14)(q13;q11)
12	34	19w+	46,XN,t(4;20)(q21;q13.3)	Biochemical abnormal screening	Normal
13	34	19w+	46,XN,t(5;11)(p14;p15)	History of fetus with Down syndrome and congenital anomalies	46,XY,t(5;11)(p14;p15)
14	32	20w+	46,XN,t(5;11)(p15;q13)	Biochemical abnormal screening	
15	30	18w+	46,XN,t(5;13)(q13;q12)	Biochemical abnormal screening	46,XY,t(5;13)(q13;q12)
16	27	20w+	46,XN,t(5;20)(q13;q12)	History of fetus with chromosome anomalies	46,XY,t(5;20)(q13;q12)
17	31	18w+	46,XN,t(10;19)(q24;p13.1)	Parent with abnormal karyotype	46,XY,t(10;19)(q24;p13.1)
18	36	21w+	46,XN,t(17;19)(p11;q13)	Advanced maternal age	
19	30	19w+	46,XN,t(17;22)(q21;q11)	Parent with abnormal karyotype	
20	34	21w+	46,N,t(X;1)(p11;q11)	Biochemical abnormal screening	
21	36	18w+	46,XN,der(18)t(5;18)(p13;p11)	Advanced maternal age	46,XY,t(5;18)(p13;p11)
22	24	18w+	46,XN,+18,der(18;18)(q10;q10)	Ultrasound markers	
23	27	22w+	46,XN,der(14;21)(q10;q10),+21	Biochemical abnormal screening	
24	29	18w+	46,XN,+21,der(21;21)(q10;q10)	Biochemical abnormal screening	
25	23	18w+	46,XN,+21,der(21;21)(q10;q10)	Biochemical abnormal screening	
26	27	21w+	46,XN,+21,der(21;21)(q10;q10)[10]/46,XN[40]	Biochemical abnormal screening	
27	41	20w+	47,XN,?t(3;19)(q12;q13),+mar	Advanced maternal age	Normal

ic t(11;17) concurrent existence of a normal cell population (Case 2). The 2 mosaic translocations both found in adult males, and one with infertility and the other with his wife experienced recurrent miscarriages. The 7 complex translocations found in 6 adults and 1 child, composing 3 balanced reciprocal translocations involved three chromosome and three breaks (Cases 3, 4, and 5), 1 balanced reciprocal translocation with concurrent existence of an inversion (Case 6), 1 balanced reciprocal translocation with concurrent existence of a Robertsonian translocation (Case 7), and 2 trisomy 21 with concurrent existence of non-contributory balanced reciprocal translocation (Case 14 and 18). Of the 12 individuals with unbalanced translocations, 5 were adults (Case 8, 9, 10, 11, and 12) and 7 were newborns and children (Case 13, 15, 16, 17, 19, 20, and 21). The 5 adults were males with infertility and the 7 newborns and children who were suspicion of Down syndrome with unbalanced ROBs involving chromosome 21.

The total 27 cases of translocations detected in prenatal cases were shown in **Table 5**, which including 20 balanced translocations (Case 1-20), 5 unbalanced translocations (Case 21 with unbalanced t(5;18) involving chromosome 18, Case 22 with a derivative 18, Case 23-25 with unbalanced ROBs involving chromosome 21), 1 case being both unbalanced and mosaic translocation (Case 26), and 1 complex translocation with balanced t(3;19) and a marker chromosome (Case 27). In the 14 translocations with parental karyotype, 3 originated from maternal translocations, 9 originated from paternal and 2 were *de novo*.

Discussion

We analyzed translocations from 17,991 postnatal cases for the referral reasons of infertility, miscarriage, malformed childbearing history and congenital anomalies. At the same time, translocations were identified in the 4198 prenatal cases for the indications of AMA, abnormal ultrasound findings, biochemical abnormal screening, parent with abnormal karyotype, previous abnormal child and others. In the present study, we identified 254 translocations in the total cases. The incidence of translocations in postnatal cases was 1.26%, and 0.64% in prenatal cases, that was higher than in the general population (0.178%) [1].

Of the 227 translocations found in postnatal diagnosis, 18 cases were identified in the cases with congenital anomalies (the highest frequency of 2.04%), including 9 balanced translocations (1.02%) and 9 unbalanced/complex translocations (1.02%). Unbalanced translocations lead to monosomy and trisomy for segments of different chromosomes and account for ~1% of cases of developmental delay and intellectual disability [11]. Although balanced translocation carriers usually have normal phenotype, a small portion of abnormal phenotypes were described in some balanced translocations [12]. Our study was consistent with the literature report. 2 of the 9 balanced translocations involved X chromosome manifested primary amenorrhea. Therman E et al reported that the region of Xq13-Xq27 was critical to the maintenance of ovarian function and normal reproductive lifespan [13]. And the breakpoints on X chromosome in our cases were just the Xq22 and Xq24.

For the referral indications of infertility, the total frequency of translocations was 1.06%. In the male cases, the frequency of translocations was 1.32% and 0.71% for the female cases. There was a significant difference in the incidence between male and female carriers for the reason that males bearing translocations were oligozoospermic or azoospermatic due to spermatogenic disturbance [14]. Most researchers have reported that in couples with RPL, the number of female carriers of balanced chromosomal aberrations exceeded that of males significantly [15-17]. For our data of the cases with recurrent miscarriages, the frequency of female translocations (2.11%) was higher than males (1.39%), though the difference had no significance, and the total incidence of translocations was 1.75%. It is generally accepted that balanced translocations do not only lead to RPL but also increase the frequency of bearing a malformed child, and in the present study, the incidence of translocation was 0.74% in the cases for the indication of previous abnormal offspring.

206 of the 227 translocations were apparently balanced. Apart from 9 balanced translocations with congenital anomalies, the others were faced the problems on reproductive failures. The most common recurrent translocations involved the acrocentric chromosome 14 and 13, while chromosome 1, 3, 4 and 11 also

generated recurrent translocations in our results. It was not completed consistent with the early report because of different indications for cytogenetic analysis [8]. There were 14 cases with unbalanced translocations, excepted for the 9 cases with congenital anomalies, and the other 5 cases were manifested infertility. The reason for their normal phenotypes maybe there was no critical genetic information on the loss or gain segments.

In our study, chromosomal translocations are represented in prenatal diagnosis with an overall frequency of 0.64%. The highest frequency of translocations was 27.78% found in the indication of parent with abnormal karyotype, followed by 3.21% found in the cases with previous abnormal childbearing. There were 8 translocations detected in these two indications, 5 cases of them being inherited from a parent, the other 3 cases being not known the origin. These cases, in which one of the parents was carrier of a balanced chromosomal rearrangement, underwent genetic counseling in order to be informed about the recurrence risk, but also about their reproductive options. They were informed that the risk estimation for a future pregnancy is mainly empirical. The couples ascertained after having an affected baby with an unbalanced karyotype have a higher risk (20-22%) as compared with the couples identified with balanced translocations after recurrent miscarriages (2-5%) [18].

Overall, 20 translocations detected in the prenatal cases were in a balanced state and 7 cases were in an unbalanced state. Of the 7 unbalanced translocations, 4 cases with translocation trisomy 21 (Down's syndrome), 2 cases with a derivative chromosome 18 for one inherited from a parent, and 1 case with a marker chromosome apart from a de novo translocation (3;19). It's a pity that the origin of 5 unbalanced translocations was unknown. The population risk for trisomy 21 is 1 in 700 births but some couples are at a much higher risk owing to parental translocation or mosaicism [19]. For our results, the indications of the 7 detected unbalanced translocations were biochemical abnormal screening, advanced maternal age, and ultrasound markers. It was noted that if the same (balanced) karyotype found in the carrier parent was detected at prenatal diagnosis, there was no increased risk of phenotypic abnormality in the child. So in this study, the prenatal cases with an inherited balanced translocations were chosen to continue the pregnant, the cases with unknown origin translocations were given the recommendation of independent choices. Apparently, the unbalanced cases were suggested to give up the present pregnant.

In conclusion, the reproductive failure was also the major indication for detecting chromosome translocations in postnatal diagnosis. And the unbalanced translocations were mostly found in the postnatal cases with congenital anomalies, but some balanced translocations could also found in these ones. For the prenatal diagnosis, the highest frequency of translocations was detected in the indication of parent with abnormal karyotype. Most of the prenatal chromosome translocations were the result of familial translocations. For the unbalanced translocations, trisomy 21 was the most common karyotype. We encourage careful consultation for couples with chromosome translocations regarding further genetic tests, including amniocentesis, since abnormal translocation may cause loss or increase of genetic material and it shows a significantly higher abnormality rate than other indications for amniocentesis.

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Disclosure of conflict of interest

None.

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References

[1] De Braekeleer M and Dao TN. Cytogenetic studies in male infertility: a review. Hum Reprod 1991; 6: 245-250.

[2] Van Assche E, Staessen C, Vegetti W, Bonduelle M, Vandervorst M, Van Steirteghem A and Liebaers I. Preimplantation genetic diagnosis and sperm analysis by fluorescence in-situ hybridization for the most common reciprocal

translocation t(11;22). Mol Hum Reprod 1999; 5: 682-690.
[3] Roux C, Tripogney C, Morel F, Joanne C, Fellmann F, Clavequin MC and Bresson JL. Segregation of chromosomes in sperm of Robertsonian translocation carriers. Cytogenet Genome Res 2005; 111: 291-296.
[4] Nussbaum RL, Mclnnes RR and Willard HF. Thompson & Thompson Genetics in Medicine. Philadelphia, Saunders Publ. Corp.; 2007.
[5] De Braekeleer M and Dao TN. Cytogenetic studies in couples experiencing repeated pregnancy losses. Hum Reprod 1990; 5: 519-528.
[6] Ou Z, Stankiewicz P, Xia Z, Breman AM, Dawson B, Wiszniewska J, Szafranski P, Cooper ML, Rao M, Shao L, South ST, Coleman K, Fernhoff PM, Deray MJ, Rosengren S, Roeder ER, Enciso VB, Chinault AC, Patel A, Kang SH, Shaw CA, Lupski JR, Cheung SW. Observation and prediction of recurrent human translocations mediated by NAHR between nonhomologous chromosomes. Genome Res 2011; 21: 33-46.
[7] Robberecht C, Voet T, Zamani Esteki M, Nowakowska BA and Vermeesch JR. Nonallelic homologous recombination between retrotransposable elements is a driver of de novo unbalanced translocations. Genome Res 2013; 23: 411-418.
[8] Edelmann L, Spiteri E, Koren K, Pulijaal V, Bialer MG, Shanske A, Goldberg R and Morrow BE. AT-rich palindromes mediate the constitutional t(11; 22) translocation. Am J Hum Genet 2001; 68: 1-13.
[9] Kim SR and Shaffer LG. Robertsonian translocations: mechanisms of formation, aneuploidy, and uniparental disomy and diagnostic considerations. Genet Test 2002; 6: 163-168.
[10] Shaffer LG, Slovak ML and Campbell LJ. International Software Consulting Network (ISCN). An international system for human cytogenetic nomenclature. Basel, S Karger; 2009.
[11] Shao L, Shaw CA, Lu XY, Sahoo T, Bacino CA, Lalani SR, Stankiewicz P, Yatsenko SA, Li Y, Neill S, Pursley AN, Chinault AC, Patel A, Beaudet AL, Lupski JR, Cheung SW. Identification of chromosome abnormalities in subtelomeric regions by microarray analysis: a study of 5,380 cases. Am J Med Genet A 2008; 146: 2242-2251.
[12] Choi BH, Kim UH, Lee KS and Ko CW. Various endocrine disorders in children with t(13;14)(q10;q10) Robertsonian translocation. Ann Pediatr Endocrinol Metab 2013; 18: 111-115.
[13] Therman E, Laxova R and Susman B. The critical region on the human Xq. Hum Genet 1990; 85: 455-461.
[14] Van Assche E, Bonduelle M, Tournaye H, Joris H, Verheyen G, Devroey P, Van Steirteghem A and Liebaers I. Cytogenetics of infertile men. Hum Reprod 1996; 11 suppl 4: 1-26.
[15] Soh K, Yajima A, Ozawa N, Abe Y, Takabayashi T, Sato S, Sou S and Suzuki M. Chromosome analysis in couples with recurrent abortions. Tohoku J Exp Med 1984; 144: 151-163.
[16] Campana M, Serra A and Neri G. Role of chromosome aberrations in recurrent abortion: a study of 269 balanced translocations. Am J Med Genet 1986; 24: 341-356.
[17] Petrosky DL and Borgaonkar DS. Segregation analysis in reciprocal translocation carriers. Am J Med Genet 1984; 19: 137-159.
[18] Franssen MT, Korevaar JC, van der Veen F, Leschot NJ, Bossuyt PM and Goddijn M. Reproductive outcome after chromosome analysis in couples with two or more miscarriages: index [corrected]-control study. BMJ 2006; 332: 759-763.
[19] Conn CM, Cozzi J, Harper JC, Winston RM and Delhanty JD. Preimplantation genetic diagnosis for couples at high risk of down syndrome pregnancy owing to parental translocation or mosaicism. J Med Genet 1999; 36: 45-50.