Contents lists available at ScienceDirect

Asian Pacific Journal of Reproduction

Journal homepage: www.elsevier.com/locate/apjr

Document heading 10.1016/S2305-0500(13)60080-9

Major translocations in genetic counselling

József Gábor Joó*, Ákos Csaba, Zsanett Szigeti, Judit Nagy Oroszné, János Rigó jr.

Department of Obstetrics and Gynecology, Semmelweis University Medical School, Budapest, Hungary

ARTICLE INFO

Article history:
Received 2 August 2012
Received in revised form 5 August 2012
Accepted 10 September 2012
Available online 20 September 2012

Keywords:
Translocation
Balanced
Unbalanced
Karyotyping
Fetal echocardiography
Patient´s history
Serum-alfa fetoprotein screening,

ABSTRACT

Objective: To review major chromosome translocation, with special regard to the clinical differences between balanced and unbalanced, as well as de novo and inherited cases. **Methods:** The authors have included cases of major chromosome translocations detected during a 20-year period. Among the 28 cases, 25 patients carried balanced and 3 were affected by unbalanced translocations. **Results:** In cases of balanced translocation, maternal age ranged between 26 and 42 years, with a median age value of (30.5±2.67) years, while in unbalanced translocations the values were between 24-37 with a median age of (30.5±4.59) years. In three cases (13%) of balanced translocations in the patient's history previous chromosomal aberrations had been recorded. In nine cases of the same group (39%) previous miscarriages were reported. In cases in which balanced translocation was suspected, karyotyping was done in the 16th-23rd gestational weeks. In three cases of unbalanced translocation, karyotyping was performed in weeks 18 or 19. Among the 28 cases examined by us, 12 carried reciprocal and 16 were affected by Robertsonian translocations. If the involvement of chromosomes in balanced translocations was concerned, chromosome 14 was found to be overwhelmingly affected. In 14 of the 25 cases (56%) examined by us, this chromosome was definitely affected by translocation. Frequently occurring translocations in chromosomes 1, 13 and 22 are also worth mentioning. **Conclusions:** Ultrasonography performed after karyotyping-in the cases of balanced translocations-and the results of fetal echocardiography-if such imaging was done at all-provide important information about the prognosis of the fetus. In case of sonographically normal fetal anatomy the good outcome of pregnancy is probable, while in cases of unbalanced translocations the sonography reconfirms the chances of poor outcome.

1. Introduction

Chromosomal aberration is a change in the genetic substance and is accompanied by the increase, absence or translocation of the chromosomal set detectable under the optical microscope. In case excess or shortage in an individual's chromosome set is detected, the condition is known as a chromosomally unbalanced one, while the presence of a structurally rearranged but quantitatively complete physiological chromosomal set in the genome is defined as a chromosomally balanced one. Accordingly, numerical and structural chromosomal aberrations are distinguished[1]. Structural chromosomal aberrations develop after chromosomal breakage. In a translocation two chromosomes are simultaneously affected by a breakage and the broken ends are attached to the free site on the other chromosome. Such a structural rearrangement is not accompanied by loss of the genetic substance, therefore it is regarded to be a "balanced translocation", in which the patients are considered clinically healthy. However, a condition like this carries a higher risk for a chromosomally unbalanced state in the offspring (22%-39%)[2]. By type, reciprocal translocations (incidence rate: 1:500-625[3,4] and Robertsonian translocations (centric fusion) are distinguished (incidence rate: 1:900[4]). In the former, part of one non-homologous chromosome is exchanged with a part of a separate non-homologous chromosome. In the latter, centric fusion takes place between two acrocentric chromosomes, following breakages at the centromere. As far as genetic counselling is concerned, it is important to know that, in contrast with the theoretically expected two thirds, just 10% of the offsprings of patients with reciprocal translocation are affected. In Robertsonian translocations,

*Corresponding author: József Gábor Joó, MD, PhD, Department of Obstetrics and Gynecology, Semmelweis University Medical School, Budapest, Hungary.
E-mail: joogabor@hotmail.com

too, a very small proportion of the expected two thirds get diseased indeed.

The prevalence of balanced translocations at birth is 1.6–3.4/1000[4–7]. Seventy per cent of such chromosomal translocations is inherited, while approximately 30% emerges de novo[7]. Balanced and unbalanced translocations have been found in a ratio of 1.4 to 1.0[8].

Approximately 4%–5% of habitual miscarriages can be traced back to structural chromosomal aberrations[4,5,9,10]. Among unbalanced translocations, centric fusion involves the trisomy of chromosomes in groups G and D, in the first place. In the case of reciprocal translocations, however, monosomy or trisomy of the affected chromosomal segment is identified. The incidence of balanced translocations in miscarried abortuses was found approx. 1.5%. Based on the above, and after the exclusion of other possible causes, the protocol of investigating habitual miscarriages should include the karyotyping of both members of the couple since habitual miscarriages may be associated with carrying a balanced translocation[2] and it might be of great importance to learn about it prior to another pregnancy.

Certain malignant tumours, especially some haematologic[11] and lymphatic ones, relatively often combine with chromosomal translocation aberrations. In the case of chronic myeloid leukaemia, a high incidence of translocationt[6,12] (Philadelphia chromosome) has been found[13] and the literature also includes much information about chromosomal translocations associated with acute lymphoid leukaemia[5,11].

2. Material and methods

In the current study, we have included cases of major chromosome translocations detected at the Genetic Counselling Unit of the 1st Department of Obstetrics and Gynecology, Semmelweis University Medical School in the period between 1990 and 2010. Among the 28 cases, 25 patients carried balanced and 3 were affected by unbalanced translocations.

Fetal karyotyping was done via genetic amniocentesis or chorionic villi sampling. Parental karyotyping was performed by drawing blood and subsequent lymphocyte culturing. (In one of the 28 cases, the procedure also involved lymphocyte culturing, on the 6th postnatal week, following the neonatal examination.) The samples were processed at the Genetic Laboratory of our Department.

Both ultrasonography before and after karyotyping, and echocardiography were done at the Ultrasonography Laboratory of our Department.

It was the Fetopathological Laboratory of the department that did the fetopathological investigations.

3. Results

Tables 1 and 2 sum up the major demographic features in the aberrations in question and the patients' histories. Examining the 25 cases of balanced translocation, we found maternal age ranging between 26 and 42 years, the

Table 1
Major demographic features and previous histories in balanced translocations.

No.	Maternal age (year)	Gravidity	History
1	29	II	Spontaneous abortion: I (grav.s. 8)
2	38	IV	Interruption: III
3	37	IV	P: III (live, mature, healthy newborns)
4	36	III	P: II (live, mature, healthy newborns)
5	32	II	Spontaneous abortion: I (grav.s. 9)
6	40	III	P: II (live, mature, healthy newborns)
7	32	IV	P: 1989 (baby boy with 21–trisomy) 1991 (live, mature, healthy baby girl)
8	38	V	P: II (live, mature, healthy newborns); Abortion:1998 grav. s. 20 (univentricular heart)
9	36	I	(negative history)
10	29	III	P: 1988 (live, mature, healthy baby girl); 1989 [45,XY t(3;14)–balanced translocation] live, mature, healthy newborn
11	27	II	Spontaneous abortion: I (grav.s.10)
12	31	IV	P: III (live, mature, healthy newborns)
13	38	IV	P: III (live, mature, healthy newborns)
14	34	III	P: II (live, mature, healthy newborns)
15	42	IV	P: III (live, mature, healthy newborns)
16	41	IV	P: II (live, mature, healthy newborns); Spontaneous abortion: I (grav.s.8)
17	39	III	P: II (live, mature, healthy newborns)
18	27	VI	P: I (live, mature, healthy newborn); Spontaneous abortion: IV (grav.s.7–11.)
19	41	V	P: II (live, mature, healthy newborn); Spontaneous abortion: II (grav.s.8–9)
20	36	II	P: I (live, mature, healthy newborn)
21	35	V	P: I (live, premature, healthy newborn); Spontaneous abortion: III (grav.s.7–10)
22	31	III	P: I (46,XY; +4q –unbalanced translocation; died at two) Spontaneous abortion: I (grav.s.17.)
23	30	II	Spontaneous abortion: I (grav. s. 12.)
24	26	II	P: I (died on 4th postnatal week, maple syrup disease)
25	32	I	(negative history)

Table 2
Major demographic features and previous histories in unbalanced translocations

No.	Maternal age (years)	Gravidity	History
1	30	III	P: I (live, mature, healthy newborn); Spontaneous abortion: I (grav.s.13.)
2	24	I	(negative history)
3	37	I	(negative history)

median age being (30.5±2.67) years. The relevant figures in unbalanced translocations were 24–37 and (30.50±4.59) years, respectively.

As far as gravidity was concerned, primiparity was found in only 2/25 cases (8%) in balanced translocations, and multiparity (*i.e.*, four or more pregnancies in a patient's history) was recorded in 11/25 cases (44%). Two of the three unbalanced translocations (66%) affected primigravidae, the third patient was a tertiigravida. In ten of the balanced translocation cases (43%) there was no similar problem in the patient's history, while in three cases (13%), chromosomal aberrations had been recorded. In nine cases of the same group (39%) previous miscarriages were reported. (In three cases, however, the patients' obstetrical–gynecological history was completely negative.) Two of the three patients with unbalanced translocations had a negative obstetrical–genetic history, while the third one had had a miscarriage.

Maternal serum AFP screening, ultrasonography (performed in the possession of the AFP–result, but sometimes before the blood test in week 16) and, first of all, karyotyping are of special importance in the prenatal diagnostics of the aforementioned aberrations (Tables 3 and 4).

In 22 of the 25 cases of balanced translocation, the results of the maternal serum AFP test were available, the figures ranging from 0.3 to 3.0 MoM and the median value being (0.94±0.22) MoM.

Prior to karyotyping, 15 ultrasonographies were performed in the possession of the AFP–results, while in 10 cases, the

Table 3
Prenatal diagnostics in cases of balanced translocation.

No.	Maternal serum AFP (MoM)	Ultrasonography1	Gestational age (week)	Indication of karyotyping	Method of karyotyping
1	0,5	Grav.s.19. CPC of 4 mm.	19	Se–AFP+US–results	GAC
2	1,1	Grav.s.12. Normal fetal anatomy.	18	Maternal age	GAC
3	0,9	Grav.s.12. Normal fetal anatomy.	18	Maternal age	GAC
4		Grav.s.18. Normal fetal anatomy	16/20	Maternal age	CVS (at a different depart–ment) / GAC
5	0,9	Grav.s.19. CPC of 9 mm Mildly excessive amniotic fluid	20	Intermediate age +US result	GAC
6	0,9	Grav.s.12. Normal fetal anatomy.	19	Maternal age	GAC
7		Grav.s.12. Normal fetal anatomy.	18	Mother carrying trans–location, positive history	GAC
8	0,6	Grav.s.18. Normal foetal anatomy	18	Maternal age+se– AFP+positive history	GAC
9		Grav.s.13. Normal fetal anatomy	17	Maternal age	GAC
10	1	Grav.s.18. Mildly excessive amniotic fluid	18	Positive history + US result	GAC
11	1,3	Grav.s.17. Normal fetal anatomy	18	Mother carrying trans–location + paternal age	GAC
12	0,3	Grav.s.19. Normal fetal anatomy	19	Intermediate age +se–AFP	GAC
13	1,7	Grav.s.12. Normal fetal anatomy.	18	Maternal age	GAC
14	3	Grav.s.23. NT: 9 mm	23	Intermediate age + US result	CVS
15		Grav.s.13. Normal fetal anatomy	18	Maternal age	GAC
16	1,4	Grav.s.18. Excessive amniotic fluid	19	Maternal age +US result	GAC
17	0,8	Grav.s.17. Normal fetal anatomy	19	Maternal age +se–AFP	GAC
18	1,2	Grav.s.14. Normal fetal anatomy	17	Intermediate age + positive history	GAC
19	2,3	Grav.s.12. Normal fetal anatomy.	18	Maternal age +positive history	GAC
20	0,5	Grav.s.12. Normal fetal anatomy.	18	Maternal age +se–AFP	GAC
21	1,7	Grav.s.17. Normal fetal anatomy	18	Maternal age +positive history	GAC
22	1,5	Grav.s.18. Normal fetal anatomy	18	Positive history	GAC
23	1,6	Grav.s.20. Normal fetal anatomy	20	Father carrying translocation	GAC
24	1,2	Grav.s.17. Normal fetal anatomy	18	Intermediate age + positive history	GAC
25	0,78	Grav.s.18. 2–2 hyper–echogenic papillary muscles on both sides	19	US result+ se–AFP	GAC

Table 4
Prenatal diagnostics in cases of unbalanced translocation.

No.	Maternal Se-AFP (MoM)	Ultrasonography1	Gestational age (weeks)	Indication of karyotyping	Method of karyotyping
1	0,8	Grav.s.17. Normal fetal anatomy	18	Intermediate age+ se-AFP	GAC
2			In 6th postnatal week	Neonatological examination	Lymphocyte culturing
3	0,9	Grav.s.19. exces-sive amniotic fluid	19	Maternal age +paternal age	GAC

results of ultrasonographies done in gestational weeks 12-14 were available (Table 3). In six patients of the former group, ultrasonography revealed changes suggestive of possible chromosomal aberrations. All of the 10 ultrasonographies performed in gestational weeks 12-14 confirmed physiologically normal pregnancies.

In cases in which balanced translocation was suspected, karyotyping was done in the 16th-23rd gestational weeks applying genetic amniocentesis in 24 patients and chorionic villi sampling in 1 patient. (In one of the patients who underwent chorionic villi sampling elsewhere, genetic amniocentesis was performed at our department.) In 13 cases (52%), maternal age over 35 years was either the main or associated indication of chromosomal investigation. In the aforementioned six cases (24%), justified ultrasonographic changes served as the main or associated indication of karyotyping. In three cases (12%), one of the parents' being a carrier of translocation was the indication for performing the investigation.

In our three cases of unbalanced translocation, maternal serum AFP findings were available in two, the results being 0.8 and 0.9 MoM (Table 4). Also, two ultrasonographic findings prior to karyotyping were at our disposal; one of them showed normal fetal anatomy but excessive amniotic fluid. (In the third case, chromosomal aberration was merely suspected on the basis of the neonatological examination, therefore both the maternal serum AFP result and ultrasonographic findings were missing.) Karyotyping performed in weeks 18 or 19 was based on genetic amniocentesis, while in the third case, lymphocyte culturing started in the 6th postnatal week could reveal the problem. The most important findings are those of karyotyping as we are dealing with cases of chromosomal aberration (Tables 5 and 6). In interpreting them it is essential to know the parental chromosomal structures.

In two cases in the group of balanced translocations, there was no karyotyping done, but in the remaining 23 cases,

Table 5
Fetal and parental karyotypes in cases of balanced translocation.

No.	Fetal karyotype	Nature of karyotype	Parental karyotypes	
			Mother	Father
1	45,XY t(14;15)	balanced translocation	45,XX t(14;15)	46,XY
2	45,XY t(1;17)(q_{44};q_{21})	balanced translocation	45,XX t(1;17)(q_{44};q_{21})	46,XY
3	45,XY t(2;7)(q_{25};p_{21})	balanced (de novo) translocation	46,XX	46,XY
4	45,XY t(14;21)	balanced (de novo) translocation	46,XX	46,XY
5	45,XY t(13;14)(q_{11};q_{11})	balanced translocation	not tested	not tested
6	46,XY/45,XY t(14;15) (in 1 metaphase)	mosaic	46,XX	46,XY
7	45,XX t(5;18)(p_{15};q_{21})	balanced translocation	46,XX t(5;18)(p_{15};q_{21})	46,XY
8	45,XY t(14;22)	balanced translocation	46,XX	45,XY t(14;22)
9	45,XY t(13;14)	balanced translocation	45,XX t(13;14)	46,XY
10	45,XY t(3;14)(q_{29};q_{13})	balanced translocation	45,XX t(3;14)(q_{29};q_{13})	46,XY
11	45,XY t(15;22)(p_{11};q_{11})	balanced translocation	45,XX t(15;22)(p_{11};q_{11})	46,XY
12	45,XY t(14;13)	balanced translocation	46,XX	45,XY t(14;13)
13	46,XY t(1;4)(q_{22};q_{35})	balanced translocation	46,XX	45,XY t(1;4)(q_{22};q_{35})
14	45,XX t(14;22)	balanced translocation	45,XX t(14;22)	46,XY
15	46,XX t(6;7)(p_{25};q_{36})	balanced translocation	46,XX/45,XX t(6;7)(p_{25};q_{36})	46,XY
16	45,XX t(15;21)	balanced translocation	not tested	not tested
17	46,XY/45,XY t(13;8)(p_{13};q_{24})	balanced (de novo) translocation	46,XX	46,XY
18	45,XX t(3;14)(p_{21};q_{32})	balanced translocation	45,XX t(3;14)(p_{21};q_{32})	46,XY
19	45,XY t(22;14)	balanced translocation	45,XX t(22;14)	46,XY
20	45,XY t(14;18)	balanced translocation	45,XX t(14;18)/46,XX [70%/30%]	46,XY
21	46,XX t(14;18)(q_{24};q_{24})	balanced (de novo) translocation	46,XX	46,XY
22	45,XY t(1;4)	balanced translocation	46,XX	46,XY t(1;4)
23	45,XY t(1;8)(q_{32};q_{ter})	balanced translocation	46,XX	45,XY t(1;8)(q_{32};q_{ter})
24	45,XY t(13;14)	balanced translocation	46,XX	45,XY t(13;14)
25	45,XX t(4;15)	balanced (de novo) translocation	46,XX	Father: 46,XY

Table 6
Fetal and parental karyotypes in cases of unbalanced translocation.

No.	Fetal karyotype	Nature of karyotype	Parental karyotypes
1	46,XY +12p	unbalanced translocation	not tested
2	46,XY t(21;22)+	unbalanced translocation	Mother: 45,XX t(21;22) /balanced / Father: 46,XY
3	46,XY +21; t(15;13)	chromosomal aberration	Mother: 46,XX; Father:46,XY

both the mother and father's karyotypes were at our disposal (Table 5). Based on the results, in 5 cases (20%), balanced translocation in the fetus was verified with healthy parental karyotypes in the background, therefore they were regarded as "de novo" balanced translocations. In 17 cases, the aberration of the fetus happened to be a disorder it inherited from one of the parents; in two cases the parental karyotypes were not at our disposal. In one case, the fetal karyotype was regarded as clinically healthy as the translocation could only be justified in a single metaphase. Among the 28 cases examined by us, 12 carried reciprocal and 16 were affected by Robertsonian translocations. If the involvement of chromosomes in balanced translocations was concerned, chromosome 14 was found to be overwhelmingly affected. In 14 of the 25 cases (56%) examined by us, this chromosome was definitely affected by translocation. Frequently occurring translocations in chromosomes 1, 13 and 22 are also worth mentioning. At the same time, however, "unaffected" chromosomes can also be listed in association with several translocations, let us just mention chromosomes 9, 10, 11, 19 and 20. According to distribution by gender, the boy to girl ratio was found to be 18:7 (72% to 28%).

Of the three cases of unbalanced translocation (Table 6), in one case we did not have parental karyotypes at our disposal, in one of them the mother turned out to be the carrier of translocation and in the third case, the chromosomal structure of both parents were healthy. In all of the three unbalanced translocations the affected fetuses/newborns were males.

Ultrasonography performed after karyotyping–especially in balanced translocations–and the results of fetal echocardiography–if such imaging was done at all –provided important information (Table 7). The former confirmed normal fetal anatomy in the majority of the cases associated with excessive amniotic fluid in a few instances; in addition, dilated intestinal loops and hyperechogenic papillary muscles of the fetal heart were detected in one case each. Echocardiography was done in 17 of the 25 cases discussed in this study and, except for the single finding of hyperechogenic papillary muscle, fully physiological anatomy of the heart was confirmed. In pregnancies with balanced translocations, healthy newborns were delivered.

In the case of unbalanced translocations, in the newborn who was karyotyped using postnatal lymphocyte culturing, there were no ultrasonographic or echocardiographic results available, but in one of the remaining two cases complex cardiac malformation[14] and, in the other case, normal anatomy with mildly excessive amniotic fluid were found (Table 8). The latter two pregnancies were terminated by induced abortion. In one fetus, the fetopathological

Table 7
Ultrasonography after karyotyping and outcome of pregnancies in cases of balanced translocations.

No.	Echocardiography	Ultrasonography result$_2$	Outcome
1		Grav.s. 23. Normal fetal anatomy.	Delivery (live, mature, healthy)
2	No change	Grav.s.22. mildly excessive amniotic fluid	Delivery (live, mature, healthy)
3	No change	Grav.s.23. mildly excessive amniotic fluid	Delivery (live, mature, healthy)
4		Grav.s.23. Normal fetal anatomy	Delivery (live, mature, healthy)
5	No change	Grav.s.24. Normal fetal anatomy	Delivery (live, mature, healthy)
6	No change	Grav.s.22. Normal fetal anatomy	Delivery (live, mature, healthy)
7		Grav.s.23. Normal fetal anatomy	Delivery (live, mature, healthy)
8	No change	Grav.s.24. Normal fetal anatomy	Delivery (live, mature, healthy)
9		Grav.s.23. Normal fetal anatomy	Delivery (live, mature, healthy)
10	No change	Grav.s.35. Normal fetal anatomy	Delivery (live, mature, healthy)
11	No change	Grav.s.22. Normal fetal anatomy	Delivery (live, premature, healthy)
12	No change	Grav.s.24. Mildly excessive amniotic fluid	Delivery (live, mature, healthy)
13		Grav.s.22. Normal fetal anatomy	Delivery (live, mature, healthy)
14	No change	Grav.s.35. Dilated intestinal loops	Delivery (live, mature, healthy)
15	No change	Grav.s.24. Excessive amniotic fluid	Delivery (live, mature, healthy)
16	No change	Grav.s.35. Normal fetal anatomy	Delivery (live, mature, healthy)
17	No change	Grav.s.25. Excessive amniotic fluid	Delivery (live, mature, healthy)
18		Grav.s.31. Normal fetal anatomy.	Delivery (live, mature, healthy)
19		Grav.s.37. Normal fetal anatomy	Delivery (live, mature, healthy)
20	No change	Grav.s.29. Normal fetal anatomy	Delivery (live, mature, healthy)
21	No change	Grav.s.32. Normal fetal anatomy.	Delivery (live, mature, healthy)
22		Grav.s.27. Normal fetal anatomy.	Delivery (live, premature, healthy)
23	No change	Grav.s.29. Normal fetal anatomy	Delivery (live, mature, healthy)
24	No change	Grav.s.21. Normal fetal anatomy	Delivery (live, mature, healthy)
25	2–2 hyperechogenic papillary muscles	right. 2, left 1 hyperechogenic papillary muscles	Delivery (live, mature, healthy)

Table 8
Ultrasonography after karyotyping and outcome of pregnancies in unbalanced translocations.

No.	Echocardiography	Ultrasonographic result$_2$	Outcome
1		Grav.s.20. mildly excessive amniotic fluid	Induced abortion
2			Sick newborn
3	Image of complete cardiac malformation	Grav.s.23. Cardiac developmental malformation.	Induced abortion

investigation confirmed a phenotype characteristic of chromosome 21 trisomy. In the other case, mild retardation but no anatomical malformation of the fetus was found.

4. Discussion

Among the 28 cases examined by us, 25 (89%) represented balanced, while 3 (11%) were unbalanced translocations. Basically, such distribution was in agreement with the results by *Caron et al.*[15], according to which balanced translocations were more than six times more frequent than unbalances ones.

Regarding the balanced translocations in our sample, the mothers' median age was (30.5±2.67)years. *Wassman*[16] reported 34.7 years for the same parameter in his study. Having processed the details of a large sample, Hamerton *et al*. reported that in the case of balanced translocations maternal median age was (26.2±5.2) years[14]. Considering our three cases with unbalanced translocation the relevant parameter was (30.5±4.59) years, which slightly exceeded 29 years published by *Wolff et al*[2].

In balanced translocations, one or more miscarriages could be detected in 39% of our patients' history. *Wolff*reported the frequency of miscarriages in the history at 23%[2]. If the details of positive history of chromosomal aberrations were considered, the incidence rate at 13% was below the approximately 30% rate reported by *Wolff*[2].

Of the 25 cases of balanced translocation, maternal serum AFP results were at our disposal in 22 patients. Serum AFP levels fell in a range of 0.3-3.0 MoM, the median value being (0.94±0.22) MoM. In two of the twenty-two cases (9%), elevated serum AFP levels were found, which was in relatively good correlation with 14% published by *Wasmann*[16], which exceeded the elevated physiological mean for maternal serum alpha foetoprotein values. In our three cases with unbalanced translocation, one of the two available values of maternal serum AFP was within the physiological range (at 0.9 MoM), the other one was just below it (at 0.8 MoM).

We reviewed the ultrasonograms obtained in the 11-12th gestational weeks, and-in the possession of the serum AFP results-the ones taken in the 17-19th weeks of the pregnancies, with regard to the chromosomal aberrations in the focus of this study. Taking all of them, it was clear that in six of them (24%), ultrasonographic changes suggestive of some chromosomal aberration were detected. Two of them turned out to be cysts of the choroid plexus, one of them was identified as a thickened nuchal transluciency (NT). Only one of the three available ultrasonographic results of unbalanced translocations showed changes (excessive amniotic fluid could be detected).

It is important to know what (in the diagnosis of translocations) the main indication for intrauterine karyotyping was. In almost 52% of the cases, advanced maternal age was either the main or associated indication. In *Wasmann's* sample[16], the relevant figure stood at 70%. As it was mentioned earlier, chromosomal investigations were (also) necessary due to ultrasonographic changes confirmed by ultrasonography. In three further cases (12%), one of the parents was known to have been a carrier of the translocation, which explained why the invasive investigation had to be done. In two of the three cases of unbalanced translocation, we relied on genetic amniocentesis owing to the parents' age, and the mother's intermediate age in association with lower values of maternal serum AFP. In one case, postnatal examinations served as the indication for karyotyping, applying the technique of lymphocyte culturing.

In 22 of the 25 cases of balanced translocation, both parents underwent chromosomal investigations; in 5 among them, the karyotype of either parent was found healthy (de novo translocation had developed in the foetus) (26%). In 17 cases (74%), balanced translocation of one of the parents was confirmed. The ratio of inherited to de novo translocations was found 71%-29%, 72%-28% and 86%-14% in studies by *Wolff*, *Wassmann* and *Nielsen*[2,3,16], respectively. Among unbalanced translocations, one was inherited from the maternal side, the other one was a case of de novo translocation (no parental karyotyping was performed in the third case).

Considering the 28 cases representing the full sample of our investigations, 12 cases (43%) were illustrations of reciprocal translocations and 16 cases (57%) were Robertsonian ones. *Hamerton's* findings[17] were in good accordance with our own results.

In the case of inherited translocations it is important to know which of the parents has been the carrier of the chromosomal aberration in question. In our sample of 18 inherited translocations, the aberration was of maternal

origin in 12 fetuses (66%) while in six cases (33%), the father was to "blame". (We had no examples in which both of the parents were carriers of a translocation[18]; actually the statistical probability of such a case to occur is 1 in 390000 in reciprocal translocations, 1 in 810000 in centric fusion, and 1 in 560000 in "combined cases"[4]).

The literature has been widely divided about the issue of the parental origin of inherited translocations; in his sample, *Wassmann* found the aberration was of paternal origin in 56%, and of maternal origin in 44% of the cases[16] . The same was supported by findings by *Weise*[19]. According to *Hamerton*[17] and, also, *Nielsen*[3], however, slight dominance (53%) of the fathers carrying the translocation could be observed.

As far as the ratio of the foetuses by gender is considered, among the 28 cases included in our study, 21 (75%) male and 7 (25%) female fetuses/newborns were reported, that is the male to female ratio happened to be 3.0. *Nielsen*[3] also confirmed the boys' dominance in his studies, although his male to female ratio was 1.46. There are publications contradicting these figures, since *Weise*[20] reported female dominance (63%) and 0.59 male to female ratio.

We also checked which of the chromosomes were most commonly affected in the 25 cases of balanced translocation. Chromosome 14 involvement was detected in 14 cases (56%), lesser but still noteworthy frequency of involvement could be established for chromosomes 13 and 22. In all of the three cases of unbalanced translocation, different chromosomes were affected. According to *Wolff's* findings[2], too, it was chromosome 14 that was most commonly involved in cases of translocation (39%). Data in publications by *Wassmann* (37%[16] and *Nielsen* (32%)[3] also support the above.

Conflict of interest statement

We declare that we have no conflict of interest.

References

[1]Papp Z, Gardó S. *Numerical and structural chromosome abnormalities*. In: Klinikai genetika (szerk) Papp Z. Budapest: Golden Book Kiadó; 1995, p. 74–91.

[2] Wolff G, Back E, Arleth S, Rapp–Körner U. Genetic counseling in families with inherited balanced translocations: experience with 36 families. *Clin Genet* 1989; **35**(6): 404–416.

[3] Evsikov S, Cieslak J, Verlinsky Y. Effect of chromosomal translocations on the development of preimplantation human embryos *in vitro*. *Fertil Steril* 2000; **74**(4): 672–677.

[4] Campbell SA, Uhlmann WR, Duquette D, Johnson MP, Evans MI. Pregnacy outcome when both members of a couple have balanced translocations. *Obstet Gynecol* 1995; **85**(5 Pt 2): 844–846.

[5] Szabó J, Szörényi Á, Szemere Gy. Balanced translocation as an etiological factor of habitual abortion. *Orv Hetilap* 1984; **125**(2): 67–72.

[6] Hook EB, Cross PK. Rates of mutant and inherited structural cytogenetic abnormalities detected at amniocentesis: results on about 63000 fetuses. *Ann Hum Genet* 1987; **51**(Pt 1): 27–55.

[7] Jacobs PA, Frackiewicz A, Law P. Incidence and mutation rates of structural rearrangements of the autosomes in man. *Ann Hum Gen* 1972; **35**(3): 301–319.

[8] Ford CE, Clegg HM. Reciprocal translocations. *Brit Med Bull* 1969; **25**(1): 110–114.

[9] Carp H, Feldman B, Oelsner G, Schiff E. Parental karyotype and subsequent live births in recurrent miscarriage. *Fertil Steril* 2004: **81**(5): 1296–1301.

[10]Simpson JL, Bischoff F. Genetic counseling in translocations. *Urol Clin N* Am 2002; **29**(4): 793–807.

[11]Odero MD, Carlson K, Lahortiga I, Calasanz MJ, Rowley JD. Molecular cytogenetic characterization of breakpoints in 19 patients with haematologic malignancies and 12p unbalanced translocations. *Canc Gen Cytogen* 2003; **142**(2): 115–119.

[12]Sampson JE, Ouhibi N, Lawce H, Patton PE, Battaglia DE, Burry KA, et al. The role for preimplantation genetic diagnosis in balanced translocation carriers. *Am J Obstet Gynecol* 2004; **190**(6): 1707–1713.

[13]Oláh É. *Oncogenetics*. In: Klinikai genetika (szerk) Papp Z. Budapest: Golden Book Kiadó; 1995, p. 217–239.

[14]Lee ML, Tsao LY, Wang BT, Chiu IS. Maternally inherited unbalanced translocation of chromosome 22 in a 5–day–old neonate with persistent fifth aortic arch and tetralogy of Fallot. *Int J Card* 2003; **90**(2–3): 337–339.

[15]Caron L, Tihy F, Dallaire L. Frequencies of chromosomal abnormalities at amniocentesis. *Am J Med Genet* 1995; **82**(2): 149–154.

[16]Cotter PD, Caggana M, Willner JP, Babu A, Desnick RJ. Prenatal diagnosis of a fetus with two balanced de novo chromosome rearrangements. *Am J Med Genet* 1996; **66**(2): 197–199.

[17]Hamerton JL, Canning N, Ray M, Smith S. A cytogenetic survey of 14069 newborn infants. I. Incidence of chromosome abnormalities. *Clin Genet* 1975; **8**(4): 223–243.

[18]Tsuji K, Narahara K, Yokoyama Y, Ninomiya S, Kudo N, Seino Y, et al. Preproductive risk in mating between two translocation carriers: case report and review of the literature. *Am J Med Genet* 1993; **46**(5): 524–528.

[19]Weise W. Autosomale Translokationen im gynäkologisch–geburtshilflichen Krankengut–Reproduktionsverhalten und –chancen chromosmalen Translokationsträger. *Zbl Gynäkol* 1982; **104**: 321–328.

[20]Weise W. Autosomale Translokationen im gynäkologisch–geburtshilflichen Krankengut–Zytogentische Befunde. *Zbl Gynäkol* 1982; **104**: 329–342.