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Original Article

Balanced and unbalanced reciprocal translocation: An overview of a 30-year experience in a single tertiary medical center in Taiwan

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Abstract

Background: Reciprocal translocation is the most common type of translocation; however, there are only a few studies that address the indications for reciprocal translocation in amniocentesis. Here we share our data, based on 30 years' experience in a single tertiary center, to investigate the rates and indications for amniocentesis in cases of reciprocal translocations.
Methods: A retrospective review of 16,749 pregnant women, who underwent midtrimester amniocentesis between January 1981 and December 2010, was conducted. Seventy-four cases of reciprocal translocation were identified.
Results: The percentage of reciprocal translocations in all amniocentesis cases was 0.44% (74/16,749); of these 74 cases, 56 were balanced and 18 unbalanced. *De novo* abnormality occurred in 23 cases, which constituted 31.1% of all reciprocal translocations. The three major indications for amniocentesis with a diagnosis of reciprocal translocation included advanced maternal age (AMA, 52.7%), a parent with an abnormal karyotype (17.6%), and abnormal biochemical markers in the maternal serum (12.2%). For individual types of reciprocal translocations (balanced and unbalanced), except for the presence of abnormal biochemical markers in maternal serum, both AMA and a parent with an abnormal karyotype were primary indications for amniocentesis. However, the highest percentage of reciprocal translocations in all amniocentesis cases was found in cases involving a parent with an abnormal karyotype (5.16%, 13/252).
Conclusion: Patients with a parent who carries an abnormal karyotype should be encouraged to undergo amniocentesis in prenatal consultation, since the risk of a diagnosis of reciprocal translocation can be particularly high.
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Keywords: amniocentesis; reciprocal translocation; structural chromosomal abnormality

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1. Introduction

Translocations are chromosomal abnormalities that occur when chromosomes break and the fragments rejoin other chromosomes. When two nonhomologous chromosomes break and exchange fragments, new chromosomes, called derivative chromosomes, are formed. The clinical significance of translocation has been a higher risk of pregnancy wastage.[1,2] Reciprocal translocation is the most common type of translocation; it can further be classified into balanced and unbalanced rearrangements.[3] There was no loss or increase of genetic materials in balanced translocations; however, unbalanced translocations showed the opposite result.

To date, there have been few studies that address the indications for reciprocal translocation in amniocentesis, and even fewer studies discussing the predictive rate of indications for *de novo* reciprocal translocation.[5,6] A recent large series showed that advanced maternal age (AMA) was the most frequent indication for amniocentesis, which revealed a balanced reciprocal translocation,[5] and that abnormal ultrasound findings were the most frequent indications in predicting unbalanced reciprocal translocation.[6] Although the abovementioned data are available, we wanted to share our data, based on 30 years' experience in a single tertiary center,[9] and study the indications and abnormality rates of amniocentesis. Our objective was to present data on all cases diagnosed with reciprocal translocation. Finally, we summarized both data sets—those previously published and ours—and provided the largest body of domestic data as a reference, which we believe will be of great value for couples who need further genomic counseling.

2. Methods

Data were obtained from amniocentesis records of the cytogenetic laboratory at Taipei Veterans General Hospital, a tertiary medical center, for the years 1981−2010.[9] Detailed information on the indications for a prenatal diagnosis of chromosomal abnormality with cytogenetic analysis has been presented previously[7] and includes the following: (1) AMA, that is, if the mother was ≥34 years of age at the expected date of confinement; (2) abnormal chorionic villus sampling (CVS) results; (3) abnormal biochemical markers in maternal serum, such as maternal blood Down syndrome screening (≥1/270); (4) abnormal ultrasound findings; (5) an intrauterine fetal death (IUFD); (6) a family history of chromosomal abnormalities; (7) a parent with abnormal karyotype; (8) a history of abnormal offspring birth; (9) radiation or medication exposure during pregnancy; and (10) other nonspecific indications such as anxiety and consanguineous marriage.

Pieces of separate chromosomes breaking off of their original chromosomes and switching places form reciprocal translocation, which might cause loss or increase of genetic material. The frequency of reciprocal translocation and *de novo* type of reciprocal translocation in various indications was estimated as the information for genetic counseling.

3. Results

A total of 16,749 amniocentesis cases were analyzed, and 74 of them involved reciprocal translocation. The highest proportion of reciprocal translocations was found in cases with the indications of AMA (52.7%, 39/74), abnormal biochemical markers in maternal serum (12.2%, 9/74), and a parent with an abnormal karyotype (17.6%, 13/74) (Table 1). However, the proportions of reciprocal translocation were not so obvious in cases with abnormal CVS results (1.4%, 1/74), abnormal ultrasound findings (4.1%, 3/74), IUFDs (1.4%, 1/74), a family history of chromosomal abnormality (1.4%, 1/74), a history of abnormal offspring birth (1.4%, 1/74), medication or radiation exposure (2.7%, 2/74), and other nonspecific indications (2.7%, 2/74) (Table 1).

Fifty-six and 18 cases were balanced and unbalanced reciprocal translocations, respectively (Table 1). Compatible

Table 1
Frequency of reciprocal translocation according to different indications.

	Amniocentesis in different indications (number = *n*/frequency = %)										
Anomaly	Total	AMA	Abnormal CVS results	Abnormal ultrasound findings	Abnormal maternal serum marker	IUFD	Family history	Parental abnormal karyotype	Previous abnormal child	Radiation or medication exposure	Others
Reciprocal translocation											
Current study	74	39 (52.7)	1 (1.4)	3 (4.1)	9 (12.2)	1 (1.4)	1 (1.4)	13 (17.6)	2 (2.7)	2 (2.7)	3 (4.1)
Chen et al (2010, 2011)	127	47 (37.0)	0 (0)	15 (11.8)	10 (7.9)	0 (0)	0 (0)	45 (35.4)	5 (3.9)	0 (0)	5 (3.9)
Sum	**201**	**86 (42.8)**	**1 (0.5)**	**18 (9.0)**	**19 (9.5)**	**1 (0.5)**	**1 (0.5)**	**58 (28.9)**	**7 (5.0)**	**2 (1.0)**	**8 (4.0)**
Balanced reciprocal translocation											
This study	56	30 (53.6)	1 (1.8)	1 (1.8)	8 (14.3)	0 (0)	1 (1.8)	10 (17.9)	1 (1.8)	2 (3.6)	2 (3.6)
Chen et al (2010)	87	41 (47.1)	0 (0)	2 (2.3)	9 (10.3)	0 (0)	0 (0)	28 (32.2)	2 (2.3)	0 (0)	5 (5.8)
Sum	**143**	**71 (49.7)**	**1 (0.7)**	**3 (2.1)**	**17 (11.9)**	**0 (0)**	**1 (0.7)**	**38 (26.6)**	**3 (2.1)**	**2 (1.4)**	**7 (4.9)**
Unbalanced reciprocal translocation											
This study	18	9 (50)	0 (0)	2 (11.1)	1 (6.7)	1 (5.5)	0 (0)	3 (16.7)	1 (6.7)	0 (0)	1 (5.5)
Chen et al (2011)	40	6 (15)	0 (0)	13 (32.5)	1 (2.5)	0 (0)	0 (0)	17 (42.5)	3 (7.5)	0 (0)	0 (0)
Sum	**58**	**15 (25.9)**	**0 (0)**	**15 (25.9)**	**2 (3.6)**	**1 (1.8)**	**0 (0)**	**20 (34.5)**	**4 (6.9)**	**0 (0)**	**1 (1.7)**

AMA = advanced maternal age, that is, if the mother was ≥34 years of age at the expected date of confinement; CVS = chorionic villus sampling; IUFD = intrauterine fetal death.

with the above data, AMA was a major indication for amniocentesis to detect reciprocal translocations, contributing 53.6% (30/56) in cases of balanced reciprocal translocations and 60% (9/15) in cases of unbalanced reciprocal translocations (Table 1). Two other indications—abnormal biochemical markers in maternal serum and a parent with an abnormal karyotype—were also significant, since they amounted to 14.3% (8/56) and 17.9% (10/56), respectively, of all indications for amniocentesis in the detection of balanced reciprocal translocations. In contrast, an abnormal maternal serum marker was not obvious in cases of unbalanced reciprocal translocations.

In this study, AMA was the main indication for amniocentesis in the detection of *de novo* balanced reciprocal translocations (47.1%, 8/17) and unbalanced reciprocal translocations (66.7%, 4/6) (Table 2). The overall percentage of reciprocal translocations in all amniocentesis cases was 0.44% (74/16,749) (Table 3). In an evaluation of the frequency of reciprocal translocations in all indications, a parent with an abnormal karyotype had the highest percentage (5.16%, 13/252) (Table 3). None of the other indications, except abnormal CVS results and IUFDs, had a detection rate above 2%. In the evaluation of the percentage of *de novo* reciprocal translocations, only abnormal CVS results reached 4%. Since the case number for this indication was too small, compared with other indications (Table 4), the clinical significance of the results should be interpreted with caution.

4. Discussion

In this study, we found that AMA was a major indication for amniocentesis, since AMA contributed to the highest proportion of reciprocal translocations (more than one-half of cases, compared with only one-third of cases in Chen et al's study; Table 1).[5,6] However, cases involving a parent with an abnormal karyotype contributed to a similar proportion (one-third of cases) of indications for amniocentesis to detect reciprocal translocations in Chen et al's study,[5,6] but contributed to only one-sixth of the cases in this study. The reason for this discrepancy was not clear, but it might be secondary to selection bias and rapid molecular cytogenetic development (Chen was a leader in cytogenetic diagnosis). Subsequently, these two major indications (AMA plus a parent with an abnormal karyotype) covered more than 70% (70.3% in our study and 72.4% in Chen et al's studies[3]) of all cases of reciprocal translocations that were diagnosed by amniocentesis. When we summarized both data sets, we found that both AMA and a parent with an abnormal karyotype contributed to 71.7% of cases of reciprocal translocations diagnosed by amniocentesis, suggesting that these two were the most important indications for amniocentesis to detect reciprocal translocations.

The main indication for amniocentesis in Taiwan is AMA,[7−9] and this indication was found to be most important in other countries as well,[10,11] with the exception of one study.[12] AMA contributed to more than one-half of all indications for amniocentesis, ranging from 54.8% to 65.5% in Taiwan[7−9]; therefore, it is understandable that the greatest

Table 2
Frequency of *de novo* reciprocal translocation with different indications.

Authors	*De novo* case		*De novo* abnormality case (number = *n*/frequency = %)							
	AMA	Abnormal CVS results	Abnormal ultrasound findings	Abnormal maternal serum marker	IUFD	Family history	Parental abnormal karyotype	Previous abnormal child	Radiation or medication exposure	Others
Balanced reciprocal translocations										
This study	17	8 (47.1)	1 (5.9)	2 (11.8)	0 (0)	1 (5.9)	0 (0)	1 (5.9)	1 (5.9)	2 (11.8)
Chen et al (2010)	17	9 (52.9)	1 (5.9)	2 (11.8)	0 (0)	0 (0)	1 (5.9)	0 (0)	0 (0)	4 (23.5)
Sum	34	17 (50)	2 (5.9)	4 (11.8)	0 (0)	1 (2.9)	1 (2.9)	1 (2.9)	1 (2.9)	6 (17.6)
Unbalanced reciprocal translocation										
This study	6	4 (66.7)	1 (16.7)	1 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Chen et al (2011)	7	2 (28.6)	5 (71.4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Sum	13	6 (46.2)	6 (46.2)	1 (7.7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

AMA = advanced maternal age, that is, if the mother was ≥34 years of age at the expected date of confinement; CVS = chorionic villus sampling; IUFD = intrauterine fetal death.

Table 3
Frequency of reciprocal translocation with different indications for amniocentesis.

Indication	Case number (*n*)	Reciprocal translocation (*n*)	Frequency of abnormality (%)
AMA	10,970	39	0.36
Abnormal CVS results	25	1	4
Abnormal biochemical markers in maternal serum	2090	9	0.43
Abnormal ultrasound findings	484	3	0.62
IUFD	50	1	2
Family history	183	1	0.55
Parent with abnormal karyotype	252	13	5.16
Previous abnormal offspring	792	2	0.25
Radiation or medication exposure	165	2	1.21
Others	1662	3	0.18
Total	16,749	74	0.44

AMA = advanced maternal age, that is, if the mother was ≥34 years of age at the expected date of confinement; CVS = chorionic villus sampling; IUFD = intrauterine fetal death.

number of abnormality cases in amniocentesis was detected under an AMA indication. However, the frequency of abnormality seemed to be lower if we used AMA as an indication for amniocentesis, since the frequency of any chromosomal aberration was obviously lower than the frequency of other indications for amniocentesis. In our previous study,[6] the frequency of the abnormality rate was only 2.47% when we used AMA as an indication compared with 2.72% for all other indications. This finding was also confirmed by other studies (2.0% for AMA vs. 3.5% for all indications in one study[7] and 2.3% for AMA vs. 2.9% for all indications in another study[8]). In this study, we focused on the specific structural abnormality—reciprocal translocations—and also observed that only 0.36% of abnormalities were found with the indication of AMA, but an overall 0.44% were found with all other indications.

Although parents with abnormal karyotypes might not be so obvious, compared with AMA as an indication for amniocentesis in our previous study[6] or this study, the indication of a parent with an abnormal karyotype contributed to 17.6% of all cases diagnosed with reciprocal translocation. A parent with an abnormal karyotype might be a much more important indication for amniocentesis in detecting reciprocal translocation, because other studies showed a higher proportion (35.4%) for this than for all other indications for the diagnosis of reciprocal translocations,[4,5] and of great importance, this proportion was similar to that of AMA (37%), which was conventionally considered as the most important indication for amniocentesis.[4–10] In this study, we emphasize the importance of a parent with an abnormal karyotype as an indication for amniocentesis, because we found that the frequency of reciprocal translocations was much higher (5.16%, or nearly 12-fold greater) than the overall frequency of 0.44% for all indications for amniocentesis, when the indication was a parent with an abnormal karyotype. In fact, in our previous study,[6] we reported a similar finding. Although a parent with an abnormal karyotype contributed to only 1.5% of all indications for amniocentesis, the rate of chromosomal aberrations was higher, up to 11.51%, i.e., a nearly four-fold increase of the overall rate (2.72%) of any chromosomal aberration in all indications for amniocentesis. In addition, a study in 1996 proposed that the overall risk at the second trimester prenatal diagnosis was 14% (8/57) for unbalanced reciprocal translocations in cases with one of the parents as a reciprocal translocation carrier.[12] Furthermore, the frequency of *de novo* reciprocal translocations for the indication of a parent with an abnormal karyotype and for all other indications (0.13% vs. 0.14%) (Table 4) was similar, suggesting the importance of a hereditary pattern secondary to the parent. Taken together, parents with an abnormal karyotype are encouraged to undergo amniocentesis in prenatal consultation, because not only is the overall detection rate of any chromosomal aberration high, but also the detection rate for the specific type of chromosomal abnormality, for example, reciprocal translocation, is much higher.

Table 4
Frequency of *de novo* reciprocal translocation with different indications for amniocentesis.

Indication	Case number (*n*)	Reciprocal translocation (*n*)	Frequency (%)
Advanced maternal age	10,970	12	0.11
Abnormal chorionic villus sampling results	25	1	4
Abnormal biochemical markers in maternal serum	2090	2	0.10
Abnormal ultrasound findings	484	3	0.62
Intrauterine fetal death	50	0	0
Family history	183	1	0.55
Parent with abnormal karyotype	252	0	0
Previous abnormal offspring birth	792	1	0.13
Radiation or medication exposure	165	1	0.61
Others	1662	2	0.12
Total	16,749	23	0.14

The role of abnormal biochemical markers in maternal serum might be very similar to that of AMA, since the former also contributed to one-tenth of all indications for amniocentesis, and the frequency of detecting abnormality was nearly equal to all indications. For example, in all chromosomal aberrations, the rate of abnormality was 2.97%, compared with 2.72% in all indications.[6] In this study, we further confirmed this observation. Abnormal biochemical markers in maternal serum contributed to 12% of all indications for amniocentesis in diagnosing reciprocal translocations, but the frequency was only 0.43%.

The other significant difference between the current study and Chen et al's study was the abnormal ultrasound findings. In the current study, abnormal ultrasound findings contributed to less than 5% of all indications with a diagnosis of reciprocal translocation, but more than 10% in Chen et al's study.[4,5] Although the cause is not clear, the different experts in ultrasound and cytogenesis at our institute, and of course selection bias might explain this observation.

We also studied the proportion of different indications for *de novo* reciprocal translocations. A study in 1991, collecting

10-year data with 377,357 amniocentesis cases from cytogenetic laboratories in America and Canada, showed that approximately 0.47/1000 had *de novo* reciprocal translocations.[13] One study using domestic data showed that approximately 0.8/1000 had a *de novo* reciprocal translocation.[14] Another study including 29 Italian laboratories reported that approximately 0.68/1000 had a *de novo* reciprocal translocation.[15] We found a higher prevalence of *de novo* reciprocal translocation (1.4/1000) in this study (Table 4).

In conclusion, our study demonstrated that there were three major indications for amniocentesis in diagnosing reciprocal translocations. Although AMA was a leading indication for reciprocal translocation, indication of parents with abnormal karyotypes also shows high risk for this chromosome abnormality, according to our data. We encourage careful consultation for parents with abnormal karyotypes regarding further genetic tests, including amniocentesis, since abnormal reciprocal 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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