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Original Article

# Chromosomal deletions detected at amniocentesis

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ABSTRACT

*Objective:* The aim of this study is to present the incidence, prenatal and postnatal findings, and modes of ascertainment in chromosomal deletions detected at amniocentesis.
*Materials and methods:* We reviewed all the cases with chromosomal deletions, which were detected by amniocentesis in Mackay Memorial Hospital, Taipei, Taiwan, between January 1987 and December 2012. Data on the locations and types of deletion, reasons for performing amniocentesis, maternal age, gestational age at amniocentesis, fetal karyotypes, inheritance of deletions, and relative prenatal findings were collected.
*Results:* Amniocentesis was performed in 33,305 cases within this period of time. Among these, 31 cases of chromosomal deletions were considered for the study. The mean gestational age at amniocentesis was 21.0 weeks (range from 15 weeks to 32 weeks) and the mean maternal age at amniocentesis was 32.1 years (range from 26 years to 37 years). Nineteen cases (61.3%) manifested fetal structural abnormalities on ultrasound, nine (29.0%) presented no ultrasound abnormalities, and three had an unknown status. The main modes of ascertainment included abnormal ultrasound findings in 10 cases (32.2%), advanced maternal age in 11 cases (35.5%), abnormal maternal serum screening results in six cases (19.6%), and other reasons in four cases (13.0%). Of the 27 cases with known inheritance, the deletion was inherited in two (6.6%) and *de novo* in 25 (92.6%). Males accounted for 11 (35.5%) and females for 20 (64.5%) cases. Chromosomal deletions are more often to occur in chromosomal 5(4 cases, 12.9%), chromosomal 18 (4 cases, 12.9%), chromosomal 4 (3 cases, 9.7%), chromosomal 7 (3 cases, 9.7%), chromosomal 10 (3 cases, 9.7%), chromosomal 11 (3 cases, 9.7%), and chromosomal 1 (2 cases, 6.5%). There were four cases of chromosomal mosaicism: two involved chromosome 5, one involved chromosome 10, and one involved chromosome 18. Twenty-three cases (74.2%) had terminal deletions and the other eight cases (26.7%) had interstitial-type deletions.
*Conclusion:* In summary, we have presented the results of prenatal diagnosis for chromosomal deletions using amniocentesis. Chromosomal deletions are more likely to occur in females and more often in chromosomal 5p and 18q. Prenatal diagnosis at amniocentesis is frequently associated with advanced maternal age, abnormal ultrasound findings, and abnormal maternal serum screening. The frequency of ascertainment in chromosome deletion seems to be directly correlated with advanced maternal age and abnormal ultrasound findings. In cases with terminal deletions, prenatal ultrasound plays a more important role for prenatal diagnosis.


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## Introduction

Prenatal diagnosis with amniocentesis had been performed for many decades, and various types of chromosomal abnormalities were reported in several references. Deletion of a chromosome is a kind of structural aberration, which means that a portion of the chromosome is missing or deleted. There are two types of deletions: when a deletion occurs toward the end of a chromosome, we call it a "terminal deletion" and when it occurs from the interior of a chromosome, we call it an "interstitial deletion". The symbol *del* is used to denote these deletions. Amniocentesis may detect inherited or *de novo* deletions. The loss of genetic materials may cause different kinds of fetal anomalies. In this article, we present cases of chromosomal deletion from our cytogenetic laboratory in Mackay Memorial Hospital, Taipei, Taiwan.

## Materials and methods

We reviewed all the cases with chromosomal deletions, which were detected by amniocentesis in Mackay Memorial Hospital, between January 1987 and December 2012. Data on the locations and types of deletion, reasons for performing amniocentesis, maternal age, gestational age at amniocentesis, fetal karyotypes, inheritance of deletions, and relative prenatal findings were collected. Cytogenetic analyses of parental blood lymphocytes were performed in all cases. The clinical data of our study cases are summarized in Table 1 [1–19].

## Results

Within this period of time, amniocentesis was performed in 33,305 cases. Various kinds of chromosomal abnormalities were found in 967 cases; the incidence of chromosomal abnormality was 3.1%. Among these, 31 cases of chromosomal deletions were studied. The incidence of chromosomal deletion was 0.093% (about 1/1110). It accounts for only 3.2% of total chromosomal abnormalities observed by us.

Of these cases, the mean gestational age at amniocentesis was 21.0 weeks (range from 15 weeks to 32 weeks) and the mean maternal age at amniocentesis was 32.1 years (range from 26 years to 37 years). Of the 31 cases, 19 cases (61.3%) manifested fetal structural abnormalities on ultrasound, nine (29.0%) presented no ultrasound abnormalities, and three had an unknown status. The main modes of ascertainment included abnormal ultrasound findings in 10 cases (32.2%), advanced maternal age in 11 cases (35.5%), abnormal maternal serum screening results in six cases (19.6%), and other reasons in four cases (13.0%).

Of the 27 cases with known inheritance, the deletion was inherited in two (6.6%) and *de novo* in 25 (92.6%). Males accounted for 11 cases (35.5%) and females for 20 cases (64.5%). Chromosomes involved in the greatest proportion of deletions were chromosome 5 (4 cases, 12.9%), chromosome 18 (4 cases, 12.9%), chromosome 4 (3 cases, 9.7%), chromosome 7 (3 cases, 9.7%), chromosome 10 (3 cases, 9.7%), chromosome 11 (3 cases, 9.7%), and chromosome 1 (2 cases, 6.5%).

Four cases of chromosomal mosaicism were recorded: two involved chromosome 5, one involved chromosome 10, and one involved chromosome 18.

Twenty-three cases (74.2%) had terminal deletions and the other eight cases (26.7%) had interstitial-type deletions. Among the cases of terminal deletion, 16 (16/23, 69.6%) manifested fetal structural abnormalities on prenatal ultrasound, whereas four (4/8, 50%) accounted for interstitial deletion.

## Discussion

The first domestic study of amniocentesis in Taiwan was reported in 1992 by Hsieh et al [20], who showed 89 cases (2.99%) of chromosomal aberrations among their 2975 cases of amniocentesis. Out of these cases, 36 has structural aberrations, however, they did not mention about deletions. Later, Tseng et al [21] reported their 10-year experience with 7028 cases of amniocentesis and showed that chromosomal aberrations were detected in 207 cases (2.90%). The highest detection rate of chromosomal aberrations was observed in cases with abnormal ultrasound findings (8.86%). However, these two articles did not mention about chromosomal deletions.

A chromosomal deletion involves the loss of a part of chromosome and results in monosomy for that segment of the chromosome. If the deleted part is very large, it will be incompatible with survival to term of pregnancy. Any deletion resulting in a loss of more than 2% of the total haploid genome will be lethal [22]. Improved resolution of the conventional cytogenetic technique increases the detection rate of chromosomal deletions.

The incidence of chromosome deletion is very low. In 1992, Jacobs et al [23] found a prevalence of 0.014% for deletions at prenatal diagnosis. In 2009, Forabosco et al [24] observed that overall frequency of deletions was 1 out of 6800 (about 0.015%). Chang et al [25] reported 12 cases of chromosomal deletions in their 30-year experiences with 16,749 cases of amniocentesis, and the incidence was 0.072% (about 1/1397). In our cases, the incidence of chromosomal deletion was 0.093% (about 1/1110). Our frequency of deletions seems to be much higher than Jacob et al's [23] and Forasbosco et al's [24] reports, but closer to Chang et al's [25] report. Because Chang et al's [25] and our hospitals are the main referral centers in Taiwan, many cases with chromosomal abnormality and fetal anomalies are likely to be referred to these hospitals for further evaluation and management. Therefore, it is reasonable to have a higher frequency of detection with chromosomal deletions.

In Forabosco et al's [24] article, the most frequent chromosomal deletion was the terminal deletion of the short arm of chromosome 4, which was more frequent than 5p deletion. Forrester and Merz [26] reported that the greatest proportion of deletions involved chromosomes 22 (14.1%), chromosomes 4 (11.3%), and chromosomes 5 (11.3%), which were identified using a birth defects registry. In, our observation, chromosomal deletions are more often to occur in the short arm of chromosomal 5(4 cases, 12.9%) and the long arm of chromosome 18 (4 cases, 12.9%), which were more frequent than the deletion of chromosome 4 (3 cases, 9.7%). According to these reports, chromosomal deletions do not appear to affect all chromosomes equally; it seems that deletions involving chromosomes 5 and 4 are more common than others. Our cases showed that 18q deletion is relatively more frequent than other chromosomes. The higher incidence of deletion of chromosome 22 in the study of Forrester and Merz [26] may be due to their later detection at birth, such as DiGeorge syndrome.

In the collaborative study of Hsu et al [27], 555 cases were diagnosed prenatally through amniocentesis as having chromosome mosaicism and only 17 (0.31%) had deletions with mosaicism. In our series, four cases had chromosomal mosaicism, two involved chromosome 5 (Cases 7 and 8), one involved chromosome 10 (Case 16), and one involved chromosome 18 (Case 26).

With regard to sex ratio, Hook et al [28] showed that the proportion of females was greater than that of males among the unbalanced rearrangements (both inherited and mutant), whereas no obvious sex difference was observed among the