Taiwanese Journal of Obstetrics & Gynecology 57 (2018) 370–373

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Original Article

Higher male prevalence of chromosomal mosaicism detected by amniocentesis

Chen-Ju Lin [a, b, c, *], Shin-Wen Chen [a], Chih-Ping Chen [a, c, d, e, f, g], Chen-Chi Lee [a], Dai-Dyi Town [a], Wen-Lin Chen [a], Li-Feng Chen [a], Meng-Shan Lee [a], Chen-Wen Pan [a], Ku-Chien Lin [a], Tze-Tien Yeh [h]

[a] Department of Obstetrics and Gynecology, MacKay Memorial Hospital, Taipei, Taiwan
[b] Department of Medicine, MacKay Medical College, Taipei, Taiwan
[c] Department of Medical Research, MacKay Memorial Hospital, Taipei, Taiwan
[d] Department of Biotechnology, Asia University, Taichung, Taiwan
[e] School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan
[f] Institute of Clinical and Community Health Nursing, National Yang-Ming University, Taipei, Taiwan
[g] Department of Obstetrics and Gynecology, National Yang-Ming University, Taipei, Taiwan
[h] Department of Pediatrics, Kanru Clinic, Taipei, Taiwan

ARTICLE INFO

Article history:
Accepted 26 February 2018

Keywords:
Amniocentesis
Mosaicism
Prenatal diagnosis
Prevalence
Sex ratio

ABSTRACT

Objective: To present the calculated frequencies, male to female sex-ratio, and modes of ascertainments in different levels of chromosomal mosaicism (CM) detected at amniocentesis.

Materials and methods: This's a 10-years retrospective study between January 2008 and December 2017 and there were 13,752 cases of amniocentesis performed in MacKay Memorial Hospital, Taipei, Taiwan. Eight hundred and thirty four cases of CM were collected in this study. We reviewed their types of chromosomal abnormalities of mosaicism, the modes of ascertainment (including: advanced maternal age, abnormal ultrasound findings, abnormal maternal serum screening result, and other reasons), maternal age, gestational age at amniocentesis, fetal gender, and perinatal findings. After amniocentesis, *in situ* culture was performed and the results of karyotype with CM were divided in to three levels.

Results: In our sample of 13,752 amniocentesis, 834 cases with all levels of CM were collected in this study. Of them, there were 562 cases (4.09%) with level I mosaicism, 207 cases (1.51%) of level II mosaicism, and 65 cases (0.47%) of level III mosaicism (Table 1). In the group of advanced of maternal age (AMA), their calculated frequencies, 4.18% in level I, 1.46% in level II and 0.41% in level III, were very similar to those in total cases (p value = 0.206) without statistical significance. In the group of abnormal ultrasound findings, the calculated frequency was much higher in level III (0.87%), however, there was no statistical significance because of the small numbers of level III.

In our cases of amniocentesis, the case numbers of male case (50.20%) is very similar to female (49.80%), and the male to female ratio was 1.01. But, we found more cases of male with CM (444 cases) than female (390 cases). The sex-ratio in different levels' calculated frequencies of CM showed similar in level I, and male prevalence was found in level II and III with statistical significance (p value = 0.022). The male prevalence also revealed in both numerical and structural abnormalities in level II and level III, but no difference in the cases of level I.

Conclusion: In conclusion, our observation showed a novel finding of higher male prevalence of CM in level II and III, and both in numerical and structural abnormalities. It's consistent with the theory of better survival in male embryo after partial self-correction of initial chromosomal aberrations, male-specific selection against chromosomal abnormalities.

* Corresponding author. Department of Obstetrics and Gynecology, MacKay Memorial Hospital, No. 47, Minquan Road, Tamsui District, New Taipei City, Taiwan.
Fax: +886 2 28094679.
E-mail addresses: alflelin@yahoo.com.tw, alfie.cj.lin@gmail.com (C.-J. Lin).

https://doi.org/10.1016/j.tjog.2018.04.007

Introduction

Chromosomal mosaicism (CM) is a kind of biological phenomenon that the presence of two or more different cell lines in an individual from a single zygote [1]. Chromosomal mosaicism may cause a variety of clinical problems including the phenotypes of genomic imbalance (developmental delay, congenital malformations, cognitive disability, neurological impairment, etc.), a high risk of affected offspring, and reproductive problems such as infertility and recurrent pregnancy loss [2]. In early human embryo development, CM is relatively frequent, but in later period, like fetus, CM is rare. This is because of effective selection against abnormal cells (self-correction) or due to mitotic arrest and early wastage of abnormal embryos [3–5].

In cytogenetic laboratory, CM can be divided in to three levels. Level I mosaicism is referred as pseudomosaicism without any clinical significance. Level II mosaicism is usually referred as pseudomsaicism and of *in vitro* clonal origin, however, the possibility of true fetal mosaicism, 1% or less, may occur [6–9]. Level III mosaicism is usually referred as a true fetal mosaicism or simply as mosaicism [6,7,10,11]. A mitotic error in epiblast or extraembryonic epithelium may produce CM in both embryo and amniotic tissue or just confined to amniotic membrane. In contrast, an *in vitro* cell division defect may cause pseudomosaicism.

In prenatal diagnosis, CM is a huge interpretative issue and may need more effort to confirm the real condition of the fetus. In these decades, fluorescence *in situ* hybridization (FISH), quantitative Fluorescence-Polymerase Chain Reaction (QF-PCR), array comparative genomic hybridization (aCGH), single-nucleotide polymorphism array (SNP array) and next generation sequencing (NGS) had great technical advancement, and provided more different methods to confirm the findings of CM in amniocentesis.

In this study, we reviewed a 10 years-period of a single laboratory in a tertiary hospital, the cases found to have different levels of CM were collected. We will present their levels of mosaicism, calculated frequencies, sex ratio, their mode of ascertainment, and perinatal information.

Materials and Methods

This was a 10-years retrospective study between January 2008 and December 2017 and there were 13,752 cases of amniocentesis performed in MacKay Memorial Hospital, Taipei, Taiwan. Eight hundred and thirty four cases of CM were collected in this study. We reviewed their types of chromosomal abnormalities of mosaicism, the modes of ascertainment (including: advanced maternal age, abnormal ultrasound findings, abnormal maternal serum screening result, and other reasons), maternal age, gestational age at amniocentesis, fetal gender, and perinatal findings.

After amniocentesis, *in situ* culture was performed with standard protocol and the results of karyotype with CM were divided in to three levels as the criteria [12]:

Level I: when a single abnormal cell with chromosomal abnormality is found in one colony.

Level II: more than two cells with the same chromosomal abnormality are found in one colony, or the same abnormality is found in more than two colonies from one culture, and the abnormality is not seen in colonies from other independent cultures.

Level III: is defined as the detection of two or more cells with the same chromosomal abnormality distributed over two or more independent cultures.

The types of chromosomal abnormalities were divided in to numerical (include: trisomy, monosomy …) and structural (translocation, deletion, duplication, inversion, ring …, etc.) abnormalities.

Data were analyzed using standard statistics, a Chi-square test with Yates correction. The comparison of observation and expected part was made by binomial test.

Results

In our sample of 13,752 amniocentesis, 834 cases with all levels of CM were collected in this study. Of them, there were 562 cases (4.09%) with level I mosaicism, 207 cases (1.51%) of level II mosaicism, and 65 cases (0.47%) of level III mosaicism (Table 1), the total frequency of CM was 6.06%.

The modes of ascertainment, included AMA, abnormal ultrasound findings, abnormal maternal serum screening results, and other reasons (such as anxiety, family history, referral for assurance, etc.), were listed in Table 2. In the group of AMA, their calculated frequencies, 4.18% in level I, 1.46% in level II and 0.41% in level III, were very similar to those in total cases showed in Table 1. The p value was 0.206 (>0.05) in between the modes of ascertainment and showed no statistical significance. In the group of abnormal ultrasound findings, the calculated frequency was much higher in level III (0.87%), however, there was no statistical significance because of the small numbers of level III.

The numbers of gender, and male to female ratio (sex-ratio) were showed in Table 3 and Table 4. In our cases of amniocentesis, the percentage of male case (50.20%) is very similar to female (49.80%), and the male to female ratio was 1.01. Of interest, we found more cases of male with CM (444 cases) than female (390 cases). Higher male prevalence was suspected. The sex-ratio in different levels of CM were listed in Table 4. In Level I, male and female had similar calculated frequencies, however, higher male prevalence was found in level II and III, the statistical significance was found between gender and different levels of CM (p value $= 0.022 < 0.05$). In Table 5, higher male prevalence revealed in the both numerical and structural abnormalities with level II and level III, but no difference in the case of level I.

Discussion

Wilson et al. [13] reported 6000 amniocentesis in 1989, and level I mosaicism was seen in 2.5%–7% of amniocentesis, 0.7–1.1% in level II mosaicism, and 0.2% in level III mosaicism. In our study of 13,752 cases of amniocentesis, the calculated frequency of total CM was 6.06%, and our calculated frequencies in level I to III are 4.09%, 1.51% and 0.47%, respectively. Our calculated frequency in level II and level III seems much higher than Wilson's report. The possible reasons may include the improvement of equipment and technique in laboratory, the increase of assisted reproductive technology in recent decades.

In many chromosomal abnormalities, abnormal ultrasound findings or AMA were the main modes of ascertainments in prenatal diagnosis. Unlikely, the main mode of ascertainments for CM is variable. In our observation, the highest detection rate of level I was AMA (454 cases, 4.12%) and abnormal maternal serum results in level II (21 cases, 2.15%), and abnormal ultrasound finding in level III (4 cases, 0.87%). That means that the mode of ascertainments for CM may be incidental in amniocentesis.

Table 1
Case numbers of chromosomal mosaicism detected by amniocentesis.

	Level I	Level II	Level III	Total
Case number	562	207	65	834
Calculated frequency (percentage)	4.09	1.51	0.47	6.06

Data are presented with number and percentage.