Int J Biol Med Res. 2012; 3(3): 2196-2198

Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

Original article

Trisomy 16 in Products of Conception; a Two-Year Experience

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ARTICLE INFO

Keywords:
Chromosomal pattern
karyotype
trisomy
FISH

ABSTRACT

Objectives: The aim of this study is to demonstrate the most common chromosomal abnormality causing spontaneous miscarriages in first trimester pregnancies over a period of 2 years. Methods: The karyotype results of all retained products of conception sent for analysis at our Cytogenetics lab were retrospectively reviewed . Conclusions: Trisomy 16 was found to be the most common chromosomal abnormality causing spontaneousfirst trimester miscarriages The data from this study also supports the theory that fetal chromosomal abnormalities occur particularly in pregnancies that occur in women who are 35 years of age or older.

1.Introduction:

Miscarriage or spontaneous abortion is the spontaneous end of a pregnancy at a stage where the embryo or fetus is incapable of surviving independently, generally defined in humans at prior to 20 weeks of gestation(1),(2),(3). Miscarriage is the most common complication of early pregnancy (2).Most clinically apparent miscarriages (two thirds to three-quarters in various studies) occur during the first trimester (3).

Chromosomal abnormalities are the most common cause of first trimester miscarriage(4),(5). At least 50% of miscarriages are due to chromosomal factors (5). A pregnancy with a genetic problem has a 95% probability of ending in miscarriage (5). Most chromosomal problems happen by chance, have nothing to do with the parents, and are unlikely to recur (6). Chromosomal problems due to a parent's genes are, however, a possibility. This is more likely to have been the cause in the case of repeated miscarriages, or if one of the parents has a child or other relatives with birth defects (6).

The most common type of chromosome abnormality found in early miscarriages is "trisomy", a situation in which there are three instead of the normal two copies of a particular pair of chromosomes. Within this group, Trisomy 16 is the most common finding in first trimester miscarriages, accounting for about a third of all chromosome abnormalities in early pregnancy loss(7). Even though Trisomy 16 is the most common, trisomy of every chromosome has been seen in miscarriages(7, 8).The aim of this study is to demonstrate the most common chromosomal abnormality causing spontaneous miscarriages in first trimester pregnancies over a period of 2 years.

2. Materials and methods

This is a retrospective study of lab records ofchromosomal studies conducted on products of conception over a 2- year period from June2008 till June 2010 at Mount Sinai School of Medicine NY, USA.

A total of 100 cases of spontaneous first trimester miscarriages sent to our lab during that period were analyzed by G banding and a minority with Fluorescence In Situ (FISH) technique when needed. .

The samples were classified according to maternal age into 2 groups;

Group 1: Age 18-35 years.

Group 2: Age, 35-45 years

Of these 60% were 35 years of age and older (group 1).

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3. Results

The results of products of conception (POCs)were illustrated in table 1. 38% of the total revealed normal Karyotype.

62% of the total revealed abnormal Karyotype in the form of numerical and structural abnormalities.

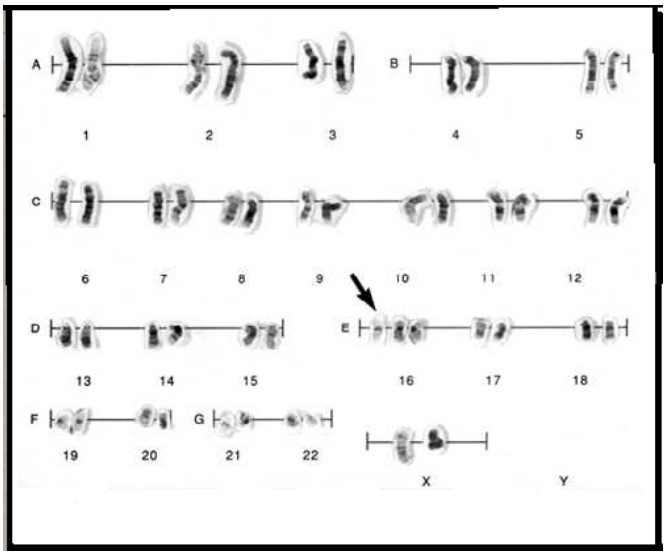
Of the abnormal Karyotype cases; 55 cases occurred in women of group 2 and 7 cases occurred in women of group 1.

The rate of trisomy 16 amongst all POCs included in the study was12%, figure one represents one of the POCs with trisomy 16 in conventional karyotyping.

Table 1: represents karyotyping pattern of POC for pregnant women of both age groups

Karyotype	No of POCs	No(%) of sera positive for IgG	
		Maternal age; Group 1	Maternal age; Group 2
46,XX	22	20	2
46,XY	16	16	0
47,XX,+7	1	0	1
47,XY,+7	1	0	1
47,XX,+8	1	1	0
47,XX,+9	1	0	1
47,XY,+9	1	0	1
47, XX,+11	1	0	1
47,XX,+14	1	0	
47,XX,+15	4	1	3
47,XY,+15	2	0	2
47,XX,+16	7	0	7
47,XY,+16	5	1	4
47,XX,+18	2	0	2
47,XY,+18	2	0	2
47,XX,+21	4	0	4
47,XY,+21	4	4	0
47,XX,+22	3	0	3
47,XY,+22	2	0	2
47,XX,inv(9)(p11;q13),+21	1	0	1
69,XXX	3	0	3
45,X	3	0	3
46,XY,inv(9) (p11;q13)	1	0	1
47,XX,+18, t(20;22) (q11.2;p11.2)	1	0	1
46,XX,i(18)(q10)	1	0	1
45,XY,-21	1	0	1
47,XY,inv(9)(p11;q13),+14	1	0	1
92,XXXX	1	0	1
69,XXX, inv(9)(p11;q13)	1	0	1
47,XX,16qh+,+20	1	0	1
69,XXY	1	0	1
46,XX,(32)/46,XY(5)	1	0	1
45,X,+21	1	0	1
47,XX,inv(9)(p11;q13),+21	1	0	1

Figure 1: A karyotype (chromosomes arrayed by size) from a POC with trisomy 16 as arrow indicates.



4. Discussion

Trisomy 16 is the most frequent autosomal anomaly seen in early spontaneous abortions, accounting for 15% of all chromosomally abnormal early spontaneous abortions and suggesting a high rate of non-disjunction of this chromosome1 (8). This trisomy is thought to be lethal in the non-mosaic state and incompatible with full fetal development (8).

What Trisomy 16 Means:

Human beings are supposed to have 46 chromosomes, which are grouped together in 23 pairs. A trisomy means that an individual has three copies of a particular chromosome instead of two. Most trisomies cause health problems of varying severity. The effects can be anywhere from mild and barely noticeable to "incompatible with life," meaning all affected babies will either be miscarried or die in early infancy (9).

Types of Trisomy 16:

A diagnosis of full trisomy 16 would mean that all the cells in the baby's body were affected by trisomy 16. Full trisomy 16 is incompatible with life and nearly all affected babies are miscarried in the first trimester (10). But it is also possible to have mosaic trisomy 16, meaning some of the body's cells are affected and other cells are normal. It is also possible, in rare cases, to have a pregnancy in which the placental cells have full trisomy 16 or mosaic trisomy 16 even though the baby is chromosomally normal (11).

Causes of Trisomy 16:

The cause of full trisomy 16 is usually an error in cell division affecting either the sperm or the egg, meaning the abnormality is already present at conception. Mosaic trisomy 16 in either the

baby or the placenta usually results from the trisomy present at conception "correcting" during cell division very early in fetal development, leaving some cells affected but not others. Researchers have not determined what causes these cell division errors but they appear to occur at random (12).

Diagnosis:

Full trisomy 16 may be diagnosed as the cause of a miscarriage if parents collect tissue and request chromosomal testing after the loss, but trisomy 16 can also be diagnosed during pregnancy through CVS or amniocentesis.

Disorders associated with chromosome 16 abnormalities include both numerical as well as structural abnormalities. Among the numerical abnormalities, full trisomy 16 is not compatible with life and is the most common chromosomal cause of first trimester abortion. Mosaicism is seen in some but not all of the cells of the affected individual's body. Whereas, a mosaic form confined to the placenta also exist in addition to uniparentaldisomy of chromosome 16. Structural abnormalities include l6p-, 16q-, l6p+, 16q+, unbalanced translocation, inversion and many other combinations of deletions and/or duplication1. This wide range of variation leads to a wide variety of outcomes, from no obvious problems to severe physical and mental handicaps, most commonly intrauterine growth retardation, congenital heart disease and developmental delay. The various outcomes may reflect the diversity of mechanisms involved in the resolution of this abnormality (12, 13).

5. Conclusions

Trisomy 16 is the most common findings in POC in our study which is consistent with other authors' findings.

Chromosomal abnormalities seem to occur in higher frequency in POC of mothers of 35 year of age and more. Further studies are needed to elucidate the exact etiology beyond these findings.

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