International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Saleem R et al. Int J Reprod Contracept Obstet Gynecol. 2024 Oct;13(10):2908-2910
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20242658

Case Report

A case report of trisomy 16 with mosaicism with intrauterine growth restriction

Raisham Saleem[1]*, Rabia Mehboob[2], Jean Aupont[3], Mustafa Ahmed[4]

[1]Department of Obstetrics and Gynaecology, Southend University Hospital, Essex, United Kingdom
[2]Department of Obstetrics and Gynaecology, Basildon University Hospital, Essex, United Kingdom
[3]Department of Obstetrics and Gynaecology, Southend University Hospital, Essex, United Kingdom
[4]Department of Fetal Medicine, Obstetrics and Gynaecology, Basildon University Hospital, Essex, United Kingdom

Received: 17 August 2024
Revised: 02 September 2024
Accepted: 03 September 2024

***Correspondence:**
Dr. Raisham Saleem,
E-mail: Raisham.saleem@nhs.net

ABSTRACT

Trisomy 16 is one the common cause of miscarriages in the 1st and 2nd trimesters. Trisomy 16 mosaicism is rarely detected by amniocentesis in the second trimester. Intrauterine growth restriction (IUGR) is one of the common outcomes of mosaic trisomy 16. Hence, we report a case of trisomy 16 mosaicism diagnosed by the cytogenetic analysis of amniotic fluid cells. The baby had an intrauterine growth restriction and interestingly her karyotype was normal. As trisomy 16 mosaic fetuses does not have a characteristic phenotype, it is recommended to inform the possibility of mosaicisms including this trisomy 16 mosaicism during prenatal genetic diagnosis and genetic counselling for parents.

Keywords: Trisomy 16, Mosaicism, Intrauterine growth restriction, Fetal anomaly, Miscarriages

INTRODUCTION

Trisomy 16 is also associated with intrauterine growth restriction (IUGR), orofacial clefting, cardiac defects, renal dysplasia, imperforate anus, and many other anomalies, but the lack of published data on the long-term outcome of these children makes it difficult to counsel parents after a prenatal diagnosis of mosaicism for trisomy 16.[1]

The major cause of trisomy 16 is an error during mechanism of mitotic nondisjunction or anaphase lag and reduction to disomy. As with many trisomic conceptuses, some full trisomy 16 embryos can undergo rescue, with the risk of residual mosaicism and uniparental disomy (UPD) for chromosome 16 in the surviving fetus. UPD can have an adverse effect on fetal development through imprinted genes, and placental mosaicism can be a cause of placental insufficiency, which can disturb fetal development.[2]

Trisomy 16 mosaicism develops through the postzygotic loss of one copy of chromosome 16, which rescues in parts of the trisomic embryo and/or placenta, and maternal uniparental disomy (UPD) is noted in approximately a third of such mosaicism cases. It is rarely observed in amniotic fluid cells, and is associated with a high risk of abnormal outcomes such as IUGR, fetal death in utero, preeclampsia, preterm delivery, neonatal death, developmental delay, congenital heart defects, and other minor anomalies.

Mosaic trisomy 16 is associated with a high risk of abnormal outcome, cases commonly exhibiting IUGR, fetal-death-in-utero, preeclampsia, preterm delivery, neonatal death, developmental delay, congenital heart defect, and other minor anomalies. This case study gives a detailed account of the detection of mosaic trisomy 16 by which several tissues from various organs were investigated and sent for cytogenetic analysis.[3]

CASE REPORT

A 28-year-old primigravida body mass index (BMI) 29.6 kg/m^2, White British, and not known to have any medical condition. Her first trimester blood biochemistry showed a low pregnancy associated plasma protein A (PAPPA), hence aspirin was offered. She had her first viability scan at 8/40 weeks that was normal. Her combined screening showed beta-human chorionic gonadotropin (B-hCG) 29.18 IU/l (0.82 MOM), PAPPA A 162.4 miu/l (0.07 MOM) NT 1.1 mm (0.7 MOM). Therefor her risk for Down syndrome was 1/370 and 1 in 22 (T13/T18). Her sonographic examination was carried out at 12 weeks showing structurally normal heart with presence of reversed A-wave in the ductus venosus showing suspicion of heart abnormality. Due to abnormal ultrasonographic studies, her echocardiography was carried out partial atrioventricular septal defect (AVSD) could not be ruled out. Her non-invasive prenatal testing (NIPT) illustrated low chances of Edwards and Patau's syndrome in this pregnancy. A repeat ultrasonography was carried out which demonstrated tricuspid regurgitation with a suspicion of ventricular septal defect at 16 weeks. Anomaly scan at 20 weeks showed strawberry shaped skull, ventricular septal defect of 1.6 mm with moderate echogenic bowels and a reduced growth velocity of less than 1.1 centile. She was offered amniocentesis which she declined. Serial growth scans were planned in view of the Intrauterine growth restriction. She later accepted amniocentesis which was carried out. Quantitative fluorescent polymerase chain reaction (QF-PCR) for chromosome 13, 18 and 21 was normal. At 21+6 weeks she was diagnosed with intrauterine fetal demise. The microarray result showed fetal karyotype 47, XY, +16/47, XY (30%/70%) confirming mosaicism trisomy 16. Specimens for karyotyping were obtained from the fetal and the placental tissues as well. The karyotypes demonstrated 47, XY, +16 for 100% in 50 metaphases of the placenta, but only 16% (10/119) in the heart. However, other specimens from cord blood, heart blood, the lung, the liver, the intestine, the brain, and the kidney were normal karyotype, 46, XY.

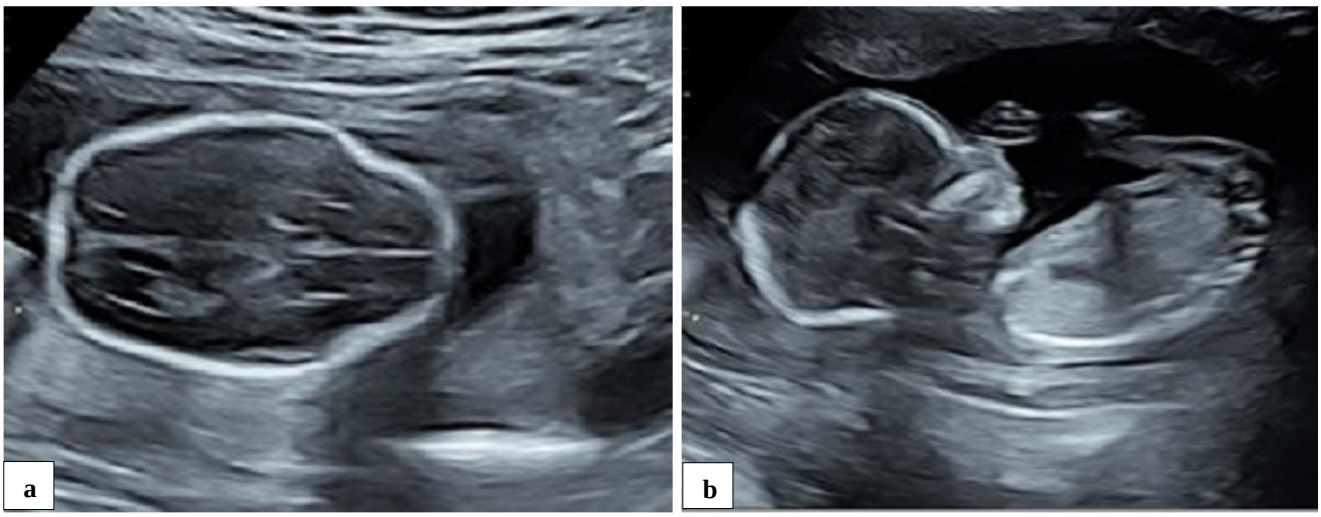

Figure 1: (a) Trisomy 16 with abnormal head shape, and (b) trisomy 16 with symmetrical IUGR.

DISCUSSION

There is an association between confined placental mosaicism (CPM) and FGR and birthweight less than 10th centile. This association is not restricted to trisomy 16, neither to CPM type 3, nor to CPM involving a meiotic trisomy. Pregnancies with all CPM types and origins should be considered to be at increased risk of FGR and low BW <10th centile A close prenatal fetal monitoring is indicated in all cases of CPM.[4] The levels of trisomy in different fetal-placental tissues are significant predictors of some measures of outcome in mosaic trisomy 16 pregnancies.[5] Analysis of reports of confined placental mosaicism for chromosome 16 without associated UPD indicates that the presence of high levels of trisomic cells in the placenta alone consistently produces a more variable inhibition of fetal growth, which may also, in cases, be associated with late pregnancy loss.[6]

An increased frequency of adverse pregnancy outcome, including pregnancy loss, intrauterine growth restriction, and premature labor, has been observed in association with CPM, which is characterized by a discrepancy between the karyotype of the fetus and placenta.[7] The association between chromosomal mosaicism observed on chorionic villus sampling (CVS) and poor pregnancy outcome has been well documented. CVS mosaicism usually represents abnormal cell lines confined to the placenta and often involves chromosomal trisomy.[8] Trisomy 16 detected at CVS may reflect the placental but not the fetal karyotype.[9] Cytogenetic discrepancies between cultured amniocytes and uncultured amniocytes may present in mosaic trisomy 16 at amniocentesis. Prenatal diagnosis of mosaic trisomy 16 should alert the association of maternal UPD 16 which may be associated with congenital heart defects and severe IUGR on prenatal ultrasound.[10] The identification of trisomy mosaicism in the prenatal setting is often shrouded

with uncertainty for the genetic counsellor, and more importantly for the parents.[11] The outcomes for these pregnancies may well be normal, but abnormalities and even in utero death are possibilities depending on the chromosomal abnormality and the degree of mosaicism.[11]

Clinicians face a dilemma following a high-risk NIPT result in the setting of normal ultrasound. Awaiting long-term culture, as opposed to short-term culture on CVS, or amniocentesis delays potential termination of pregnancy.

CONCLUSION

The number of cases of trisomy 16 mosaicism in late pregnancy or at birth are not enough to identify typical characteristics features of it. However, IUGR, aortic coarctation, congenital heart defect, intestinal atresia, craniofacial dysmorphisms, and various anomalies have been reported. In conclusion, our study revealed that this 21-week male fetus had trisomy 16, mosaic type. The trisomy 16 confined within the placenta in 100% and only 16% in the heart of fetus. The other organs revealed normal karyotype. The phenotypic features were small placenta with normal cord insertion. The fetal body showed symmetrical small gestational age without internal organ malformation.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Saleem R, Mehboob R, Aupont J, Ahmed M. A case report of trisomy 16 with mosaicism with intrauterine growth restriction. Int J Reprod Contracept Obstet Gynecol 2024;13:2908-10.