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CASE REPORT

Fetal Double Partial Trisomy 6 and 9 Due to Maternal 3:1 Meiotic Segregation of a Balanced Translocation

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SUMMARY

Background: **The aim is to investigate the origin of a rare fetal double partial trisomy 6 and 9 using CMA and guide reproductive counseling.**
Methods: **Parental karyotyping and fetal chromosomal microarray analysis (CMA) were performed to analyze chromosomal abnormalities. A literature review was conducted for similar cases.**
Results: **Parental karyotyping revealed a maternal balanced translocation, 46,XX,t(6;9)(p25;q21.1), while the fetus had 47,X?,+der(9)t(6;9)(p25;q21.1)dmat, indicating duplication 6pter→p25 and 9pter→q21.1. CMA confirmed both fragments as pathogenic copy number variations (pCNVs). This represents the first reported case of concurrent partial trisomy 6 and 9.**
Conclusions: **The aberration likely resulted from 3:1 meiotic segregation. CMA enhances detection of chromosomal abnormalities and their origins. Prenatal invasive testing remains crucial for translocation carriers.**
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KEYWORDS

double partial trisomy, CMA, balanced translocation, meiotic segregation, prenatal diagnosis

INTRODUCTION

Balanced chromosomal translocations occur in ~0.2% of individuals and are usually phenotypically benign [1]. However, carriers risk producing unbalanced gametes due to quadrivalent formation during meiosis, leading to 2:2, 3:1, or 4:0 segregation [2]. CMA is capable of analyzing genome-wide deletion/duplication, loss of heterozygosity (LOH), homozygous uniparental disomy (UPD), and paternity identification and is now widely used in the genetic diagnosis of fetal structural anomalies, polymorphisms, growth restrictions, and primary mental retardation [3].
Here, we report a rare case of fetal double partial trisomy 6 and 9 resulting from maternal 3:1 segregation, associated with cardiac and nasal bone anomalies on prenatal ultrasound.

Table 1. Overview on the 6 and 9 double partial trisomy patients reported in the literature.

Ref.	Age	Gender	Karyotype	Maternal Karyotype	Paternal Karyotype	Prenatal phenotype	Postnatal phenotype
Cetin Z	neonate	M	47,XY, der(7)t(6;7)(pter→p23:p15→>qter), +der(9)t(7;9)(pter→p15::q21.2→pter)t(6;7;9)(p23;p15;q21.2)mat	46,XX, t(6;7;9)(p23;p15;q21.2)	46,XY	at the time of his birth (G14P2Ab12) mothers and fathers ages were 39 and 44 years, respectively. The delivery was by caesarean section at term after an uncomplicated pregnancy. Birth weight was 2,300 g	congenital bilateral dislocations of the hips and dysmorphic findings were evident; microcephaly, triangular face, flat occiput, high prominent forehead, large fontanelles, microphthalmia, strabismus, blepharoptosis, low-set/malformed ears, bulbous nose, long philtrum, small mouth/thin lips, micrognathia, high arched palate, capillary hemangiomata on nose and eye-lid, deep sacral dimple, clinodactyly, brachydactyly, polydactyly on left hand, hypoplastic nails, bilateral simian crease, congenital bilateral dislocations of the hips, genu recurvatum, syndactyly between 2nd and 3rd toes, hyperextensible joints, posteriorly located anus and umbilical hernia. Cranial magnetic resonance imaging (MRI) showed hydrocephaly, colpocephaly, bilateral ventricular dilatation and hypogenesis of corpus callosum Echocardiogram revealed a ventricular septal defect and secundum atrial septal defect. Abdominal ultrasound revealed grade I hydronephrosis. Audiological examination was normal
Zhang J	5 years	F	47,XX, +der(9)?t(6;9)(q26;q21)	46,XX, t(6;9)(q26;q21)	46,XY	no abnormalities during pregnancy	full-term infant in caesarean-section birth, weight 3 kg, height 50 cm. Mental retardation, developmental retardation, epicanthus, wide eye spacing, deep eye sockets, drooping eyelids and downward corners of mouth, short to medium person, bulbous nose, low ear cupping, tooth enamel defect, speech disorder, crawling instability
our case	fetal	F	47,X?, +der(9)t(6;9)(p25;q21.1)dmat	46,XX, t(6;9)(p25;q21.1)	46,XY	absence of nasal bone, complete atrioventricular septal defect, coarctation of aorta with arch dysplasia, persistent left superior vena cava	termination of pregnancy, female, with no apparent abnormality in appearance, 900 g in weight and 35 cm in length

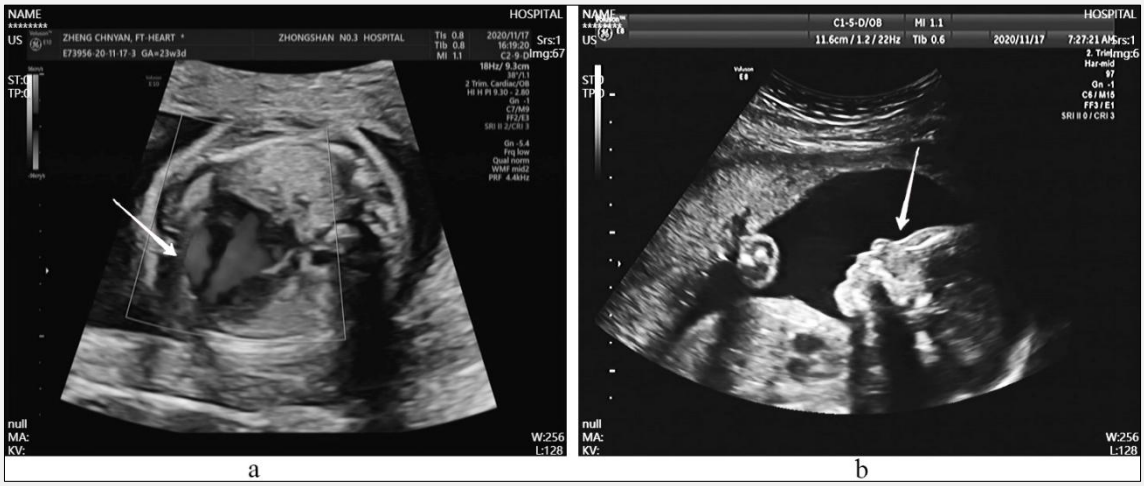

Figure 1. a - Fetal cardiac malformation (white arrow), b - Fetal absent nasal bone (white arrow).

CASE PRESENTATION

A 27-year-old primigravida with an uncomplicated pregnancy underwent routine ultrasounds. At 23+ weeks, fetal echocardiography revealed intracardiac structural abnormalities and absence of the nasal bone (Figure 1). Prenatal karyotyping identified a 47,X?, +der(9)t(6;9)(p25;q21.1)dmat with a supernumerary marker chromosome. CMA revealed two pCNVs: a 6.2 Mb duplication on arr[GRCH37] 6p25.3p25.1(108666-6305477) and a 75.5 Mb duplication on arr[GRCH37] 9p24.3q21.13(46587-75602903) (Figure 2). Parental testing confirmed a maternal balanced translocation 46, XX,t(6;9)(p25;q21.1) and a normal paternal karyotype (Figure 2), resulting in a 900 gram female stillborn with no apparent dysmorphology, autopsy was declined by the family.

We performed a comprehensive literature review (1990 - 2024) searching PubMed, CNKI, Wanfang, and Chinese medical journal databases using the terms "partial trisomy 6 and partial trisomy 9" or "6 and 9 double partial trisomy" in both English and Chinese. Only two cases of partial trisomy 6 combined with partial trisomy 9 were reported through a literature search in domestic and foreign databases, both of which were derived from maternal balanced translocations, mainly manifested as craniofacial cardiac malformations and mental retardation. The following information for each patient was reviewed: gender, karyotype, parental karyotype, and prenatal/postnatal phenotypes [4,5] (Table 1).

DISCUSSION

This report elucidates the genetic characteristics and clinical phenotypes of partial trisomy 6 and 9 syndromes. All reported cases originated from parental balanced translocations, with der(9) exclusively maternally transmitted, suggesting t(6;9) may cause infertility in male carriers [6,7]. Balanced translocation carriers form quadrivalent structures during meiosis, producing 18 possible gamete combinations, of which only normal and balanced translocation gametes are viable. Research indicates 2:2 segregation predominates (66.1%), followed by 3:1 (23.6%) and 4:0 (10.2%) separations [8]. Notably, 3:1 segregation occurs more frequently in translocations involving proximal centromeric regions on chromosome 9, with higher incidence in females than males [9-11].

Trisomy 6p syndrome manifests characteristic craniofacial dysmorphism, growth retardation, and congenital heart defects [12]. Our prenatal case only exhibited nasal bone absence and cardiac malformations. As the fourth most common autosomal trisomy after chromosomes 21, 18, and 13, trisomy 9p features intellectual disability and multiple congenital anomalies [13]. Ali Saad reported a rare case of partial trisomy 9p 13.3→pter with 22q11.1 microduplication in an 8-year-old male patient who exhibited characteristic trisomy 9p dysmorphic features but normal intellectual development. In contrast to previous reports emphasizing the 9p22 critical region, this case demonstrates phenotypic heterogeneity in partial trisomy 9p[14]. Most cases derive from parental balanced translocations, with phenotypes modified by concurrent CNVs [15]. These findings provide crucial evidence for genetic counseling.

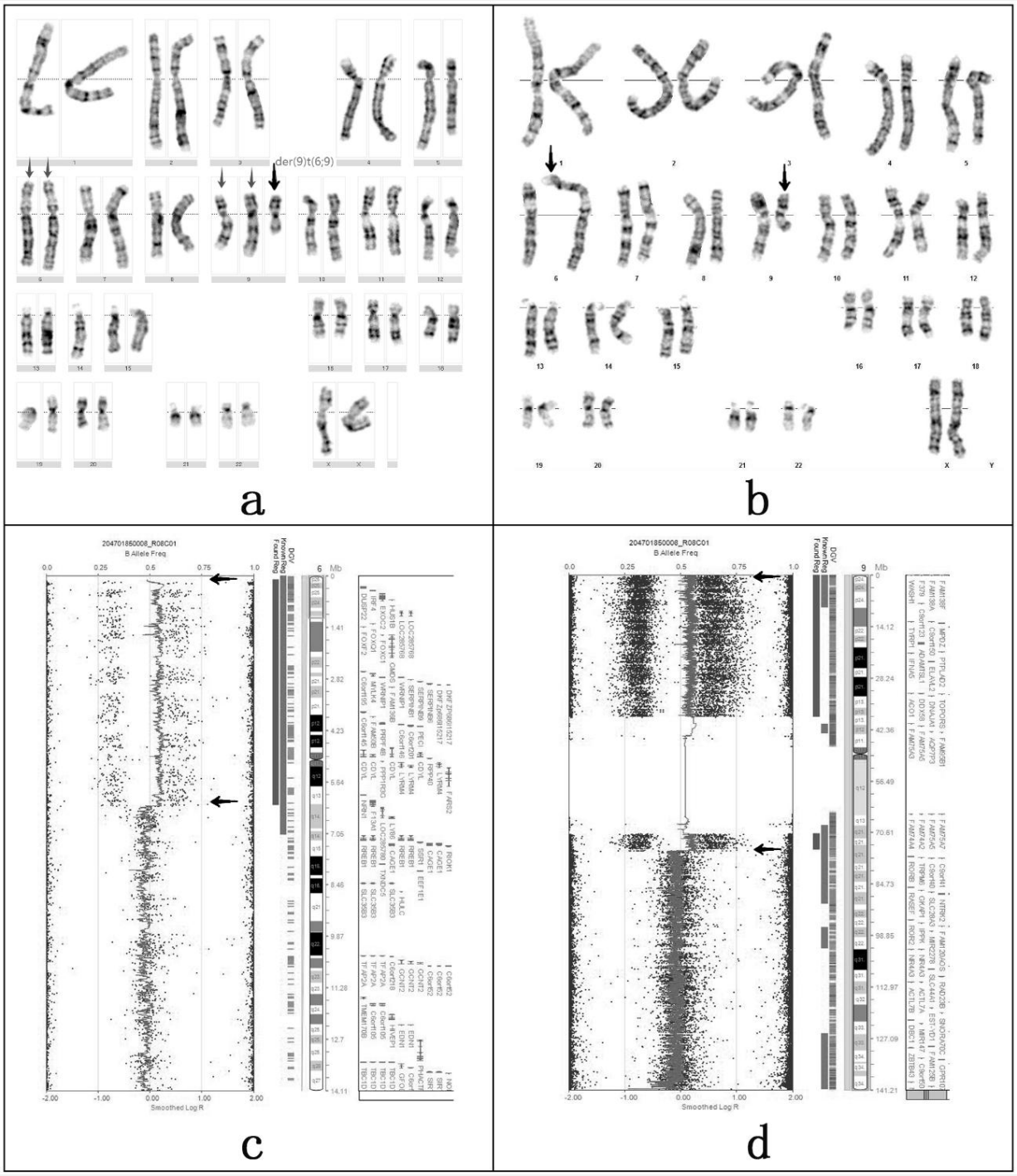

Figure 2. a: Fetal chromosome karyotype: 47,X?,+der(9)t(6;9)(p25;q21.1)dmat. Gray arrows represent normal chromosomes; Black arrow represented derived chromosome, b: Maternal chromosome karyotype: 46,XX,t(6;9)(p25;q21.1). Black arrows represent translocation chromosome, c: Fetal duplication CNV on arr[GRCH37] 6p25.3p25.1(108666-6305477). The two black arrows represented duplication CNV in 6p25.3p25.1, d: Fetal duplication CNV on arr[GRCH37]9p24.3q21.13(46587-75602903). The two black arrows represented duplication CNV in 9p24.3q21.13.

CONCLUSION

This report describes a rare case of fetal der(9)t(6;9)(p25;q21.1) caused by 3:1 meiotic segregation of a maternal balanced translocation. While concurrent partial trisomy 6 and 9 typically presents with craniofacial cardiac anomalies and neurodevelopmental impairment, these nonspecific features often emerge in late gestation. In our case, prenatal ultrasound detection of cardiac malformations led to genetic confirmation.

For patients with balanced chromosomal translocations in one spouse, prenatal diagnosis should be recommended to eliminate fetal chromosomal abnormalities and comprehensive genetic counseling about reproductive risks. The case reinforces the importance of multidisciplinary management for such pregnancies.

Acknowledgment:
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Ethics Approval:
The study was approved by the Ethics Committee of the Third Affiliated Hospital of Sun Yat-Sen University (number: CR2024-019-01).

Declaration of Interest:
The authors declare that they have no competing interests.

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