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Case Report

Monozygotic twins discordant for trisomy 21: Discussion of etiological events involved

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ABSTRACT

Objective: To elucidate the etiologies of discordant trisomy 21 in monozygotic twin pregnancy.
Case report: A monochorionic diamniotic twin pregnancy with hydrops and cleft lip (twin 1) found in one fetus presented at gestational age of 17 weeks. Amniotic fluid karyotyping showed nonmosaic trisomy 21 in twin 1 (47, XY, +21 [20]) and a normal karyotype in twin 2 (46, XY [20]). Short tandem repeat (STR) polymorphism markers revealed that the two fetuses were monozygotic, and the two chromosomes 21 were maternal isodisomy in the trisomy fetus. The chromosomal constitution of placentas in the territory of trisomy 21 cotwin was 47, XY, +21 [20] and was a mosaic 47, XY+21 [12]/46, XY [8] in the normal karyotyped twin.
Conclusion: Our case of monozygotic twin with discordant trisomy 21 might start with a prezygotic maternal meiosis II non-disjunction error-caused trisomy 21 zygote, and after twinning, one remained trisomy 21, and the other twin underwent trisomy rescue and became a mosaic trisomy 21 in morula or early blastocyst stage before the formation of pre-embryo, which subsequently resulted in mosaic trisomy 21 of the placental tissue and normal chromosomal constitution of the fetus.

Introduction

Monozygotic twins, developing from a single zygote, are almost identical in clinical phenotype and concordant in karyotypes. Monozygotic twins with discordant trisomy 21 are rare and account for about one in 385,000 cases [1]. The etiology was attributed to either originally coming from a trisomy 21 zygote due to meiosis non-disjunction then after twinning with postzygotic trisomy rescue in one fetus [2] or originating from a diploid zygote followed by post zygotic non-disjunction in one fetus after twinning [3–5]. In this case, we came across a set of monochorionic twins, where one co-twin presented with hydropic changes and cleft lip; a series of prenatal tests thus started, including amniotic fluid chromosome examination and STR analysis on amniotic fluid back-up culture and parental blood; postpartumly, chromosome check-up on fetal skin and placenta was performed. Based on the results, we sought to explore the etiological events possibly involved behind the monochorionic twin set with trisomy 21 discordancy.

Case report

A monochorionic diamniotic pregnancy occurred in a 35-year-old multigravida, nulliparous woman who conceived spontaneously. There was no known family history about trisomy. She was transferred from a local hospital due to presentation of hydrops in one twin at gestational age of 17 weeks. Sonographic examination disclosed a set of monochorionic, diamniotic twins with one fetus showing hydrops and cleft lip and another fetus as normal. Then dual amniocentesis for the two fetuses was done after sonographic exam. 20 days later, the amniotic fluid karyotyping results showed (47, XY, +21 [20]) in the hydropic fetus and (46, XY [20]) in the normal fetus. Though the single chorionicity had been confirmed

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by sonography, the rare finding of monochorionic twin with non-identical karyotyping prompted an investigation of zygosity by STR polymorphism marker analysis using the DNA from back-up amniotic fluid culture and both parents' blood as well. After genetic counseling, the parents opted for selective termination of the aneuploid fetus three days later. Unfortunately, on the morning scheduled for feticide, the trisomy fetus was found deceased in utero, while the normal co-twin suffered bradycardia. The parents had no choice but to terminate the whole pregnancy, in spite of the zygosity result still pending. Post-delivery examination confirmed a hydropic fetus with cleft lip and the other without apparent abnormalities. The placenta was monochorionic with intertwin vascular anastomoses (Fig. 1). Fetal skin and placentas from the two twins' individual territories (Fig. 1) were sent for karyotyping.

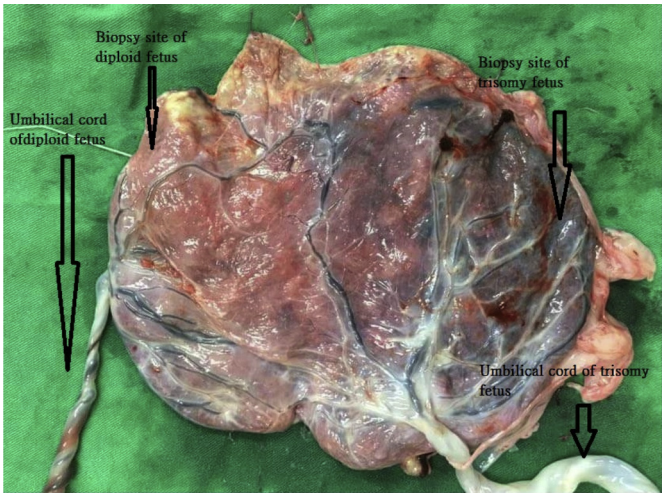

Fig. 1. Monochorionic placenta with intertwine vessel anastomoses; placental biopsies were done at each fetus' territory.

Genotyping for zygosity

All genotypes for 16 short tandem repeat (STR) markers (Amelogenin, D21S1437, D22S683, D8S1110, D10S2325, 12S1090, D17S1294, PentaD, D3S1744, D14S608, D20S470, PentaE, D4S2366, D18S536, D13S765, D6S474) were identical between the two twins, proving they were monozygotic.

Survey for extra chromosome 21

STR marker analysis of parental DNA and DNA extracted from the back-up flask of amniotic fluid culture of both fetuses was also undertaken to determine the origin of the additional chromosome 21 of the trisomy fetus. Two (D21S1435 and Penta D) of the six tested alleles (D21S1436,D21S1437, D21S1435, D21S1270, Penta D and D21S1446) were fully informative, indicating the presence of one copy of a paternally derived chromosome 21 and two identical

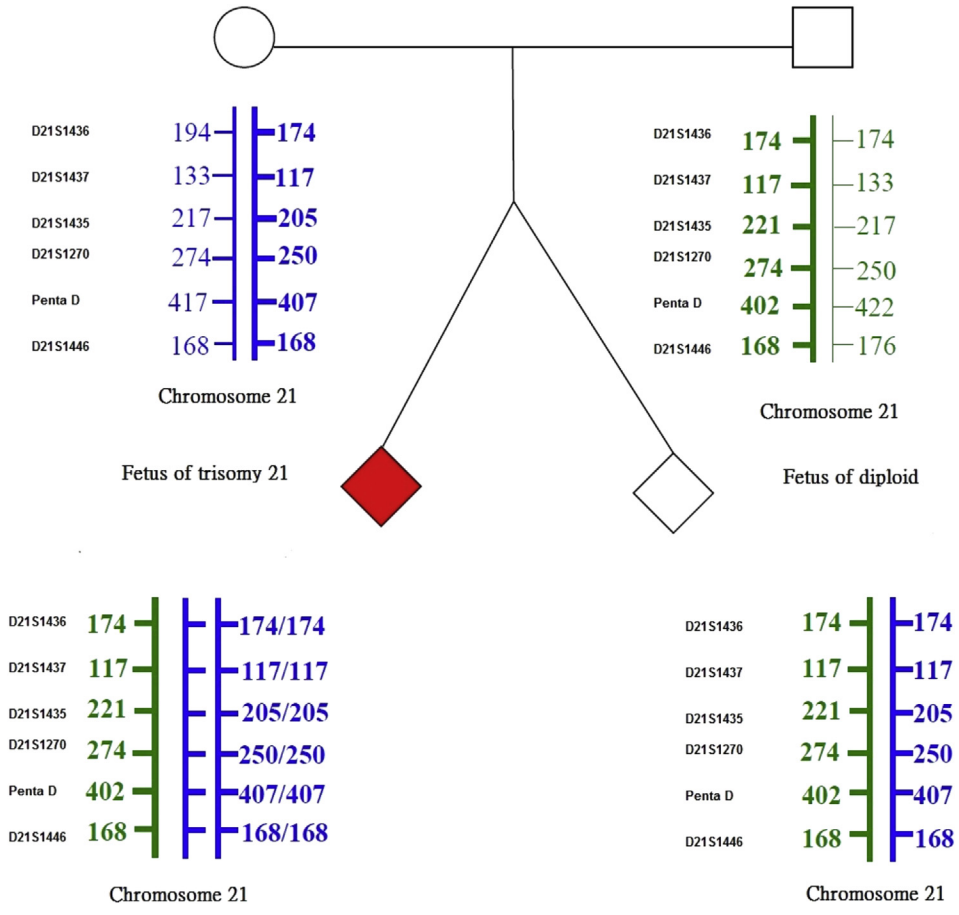

Fig. 2. Microsatellite analysis of parental DNA and DNA extracted from the amniotic fluid culture of both fetuses: The presence of one copy of a paternally derived chromosome 21 and two identical copies of a maternally derived chromosome 21 in the trisomy fetus. The additional chromosome 21 was therefore maternal in origin and there is no uniparental disomy in the normal karyotyping fetus.