

P-199 When monozygotic twins aren't identical

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1. Introduction

Monozygotic twins are considered to be genetically identical given they originate from a single egg fertilization that later splits. The chorionicity of monozygotic twins is dependent on the timing in which the twinning occurs. For monozygotic diamniotic twins, twinning typically occurs 4-8 days after conception. Thus, monozygotic twins are by definition monozygotic.¹ Additionally, at 4 days' post conception, progenitor cells of the placenta (forming trophoblast cells) become separated from the inner cell mass of the embryo¹, resulting in a single shared placenta. For this reason, many twin pregnancies determined to be identical based on chorionicity often undergo diagnostic testing for only one gestation. This case presentation demonstrates the importance of testing all gestations in multiple gestation pregnancies.

2. Methods

Clinical information, screening, and diagnostic test results were collected and evaluated on a 20-year old, G2P1 patient with a monozygotic-diamniotic twin pregnancy. Findings are presented in **Table 1**.

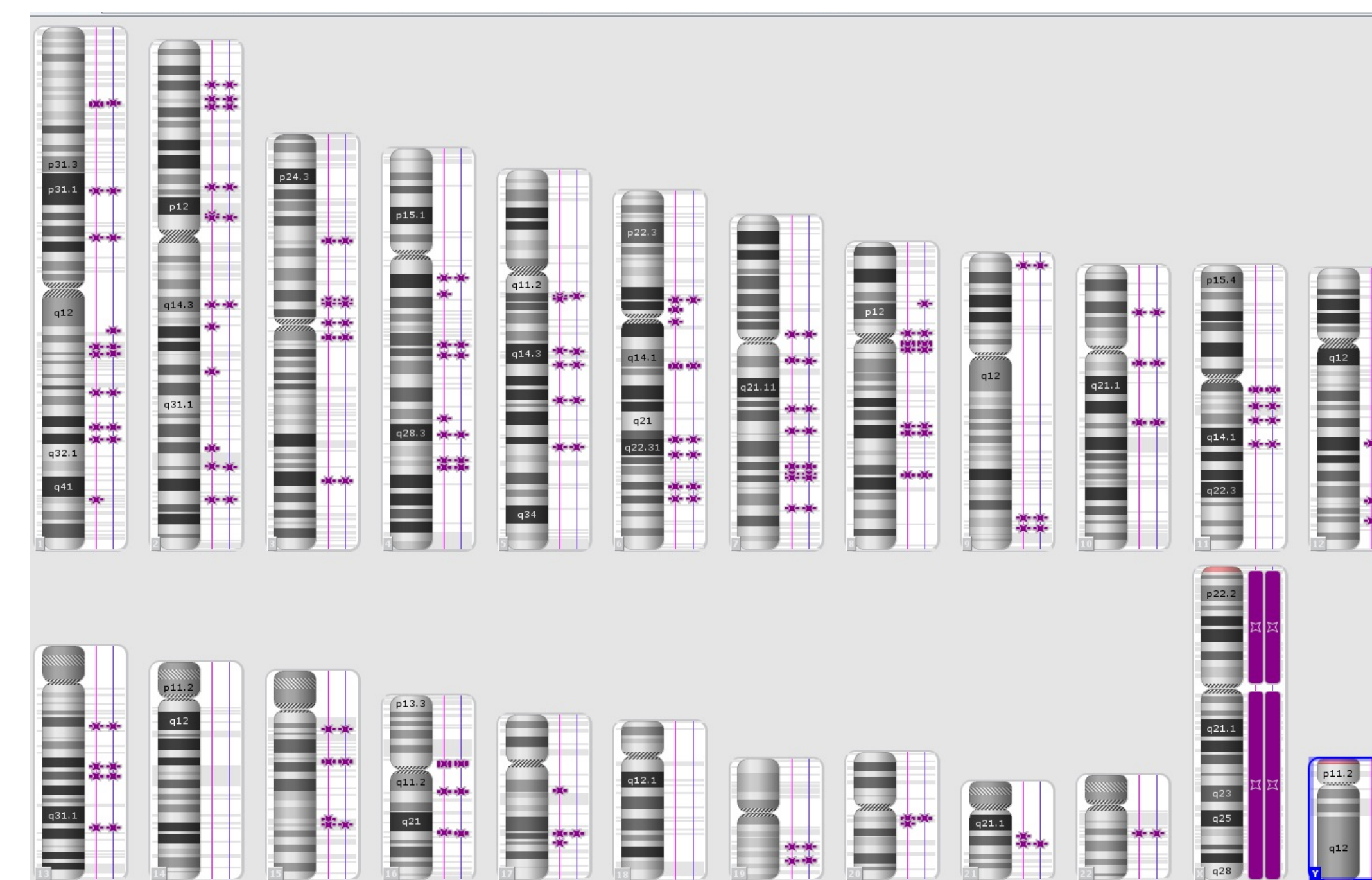
Table 1. Pregnancy findings

	Gestational Age	Results
Indication	12w0d	Ultrasound confirmation of monozygotic-diamniotic twin pregnancy. Normal NT measurements of both twins (twin A-1.5mm, twin B-1.6mm)
NIPT results	12w2d	Negative for trisomy 13, 18, 21, fetal sex consistent with male
Ultrasound	16w1d	Twin A – unremarkable Twin B – choroid plexus cysts (CPC)
Ultrasound	18w1d	Twin A – unremarkable Twin B – CPC, unilateral pleural effusion, short femur, micrognathia, pyelectasis, suspected cardiac defect
Amniocentesis	18w1d	
Aneuploidy FISH		Twin A – Normal male result Twin B – Trisomy 18
Chromosomes		Twin A – 46,XY Twin B – 47,XY,+18
Microarray		Twin A – Normal male Twin B – Gain of chromosome 18
Microarray		Comparison of SNPs within microarray data to confirm monozygosity of twins (Figure 1)
Fetal Echocardiogram	18w6d	Twin A – Normal Twin B – complex structural heart defect-atrial septal defect and ventricular septal defect; bilateral pleural effusion, umbilical artery & vein Doppler findings consistent with early hydrops
Radiofrequency ablation (RFA)	20w0d	RFA of twin B
Spontaneous delivery	39wks	Twin A delivered, 8lbs 11oz, Apgar of 8 and 9

3. Results

Ultrasound in the first trimester demonstrated a monozygotic-diamniotic twin pregnancy. Non-invasive prenatal testing (NIPT) was negative for chromosomes 13, 18, and 21 aneuploidy. After ultrasound anomalies were identified in twin B, testing of amniocytes collected from each gestational sac revealed twin A to be euploid, while twin B had trisomy 18. SNP microarray analysis was used to confirm monozygosity. (**Figure 1**)

Figure 1. SNP Microarray data: Based on the pattern of homozygosity (in purple) and statistical analysis of the SNPs by the Mendelian Error Rate (MIE), these twins are monozygotic in origin.



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4. Conclusions

Literature review indicates that the division error rates among chromosomes show increased rates of trisomy 18 post-zygotic errors (6-8%) as compared to trisomy 21 or 13.^{2,3,4} Applying this information to twin gestations, a post zygotic nondisjunction event that occurred after differentiation of cells from the trophoblast to those of the inner cell mass (~4 days' post conception) could correspond to the clinical presentation and laboratory findings seen in this case. A nondisjunction event after this differentiation could lead to aneuploidy in only one twin. Since NIPT testing utilizes circulating cell free DNA in the maternal blood largely originating from the trophoblast, negative NIPT results further support a post zygotic mitotic error in the pregnancy.

This case demonstrates several important considerations in multiple gestations, especially in relation to trisomy 18. First, when pursuing diagnostic testing, analysis of all gestations in a pregnancy is essential even in the presence of a shared placenta. Post zygotic division errors have resulted in discordant multifetal gestations, even among monozygotic gestations.^{5,6,7} Second, NIPT is limited by the source of cell free DNA and could fail to identify a post zygotic nondisjunction error. Clinical correlation of screening and diagnostic testing modalities is important. Finally, these considerations are especially important for trisomy 18, as this aneuploidy has been shown to occur as a post zygotic error more frequently than seen with trisomy 13 and 21.