When monozygotic twins aren’t identical

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1. Introduction

Monozygotic twins are considered to be genetically identical, which means they originate from a single egg and sperm cell. However, this does not entirely determine their genetic makeup. The process of development is not foolproof, and errors may occur during embryonic development, leading to differences between monozygotic twins. For example, in the first trimester of pregnancy, twins with the same chorionicity (one or two placental sacs) may develop in the same gestational sac. This can result in a single shared inner cell mass of the embryo, which can lead to genetic differences between the twins.

Additionally, at 4 days’ post conception, progenitor cells that give rise to the placenta and umbilical cord are formed. This can result in a situation where two embryos develop in the same gestational sac, leading to a single shared inner cell mass. In this case, the twins may be genetically identical. However, there is a risk of genetic differences developing due to post-zygotic errors, which can occur after the initial cell division.

2. Methods

Clinical information, screening, and diagnostic test results were collected and evaluated on a 20-year database of monozygotic twins at LabCorp. The data was collected from the 20th ISPD Annual Conference; 2022 June 19-23.

3. Results

Ultrasound in the first trimester demonstrated a monochorionic-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. SNP Microarray data: Based on the pattern of homozgyosity (in purple) and statistical analysis of the SNPs by the Mendelian Error Rate (MIE), these twins are monozygotic in origin.

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 13.2,4 Applying this information to twin gestations, a post-zygotic nondisjunction event that occurred after differentiation of cells from the trophectoderm 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.1,5,6 Second, NIPT is limited by the source of cell free DNA and may 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.

References