C-312

Whose Y is it anyway? Transplants and NIPT II

Jenna Wardrop, Samantha Caldwell, Theresa Boomer, Eyad Almasri, Ron McCullough
Sequenom Inc., a wholly owned subsidiary of Laboratory Corporation of America® Holdings, San Diego, California

Integrated GENETICS
LabCorp Specialty Testing Group
sequenom

I. Introduction

Noninvasive prenatal testing (NIPT) for fetal aneuploidies by massively parallel sequencing has emerged as a powerful tool in the management of high-risk pregnancies. It is important that patients receive pre-test counseling about the limitations of the test. Fetal sex discrepancies between NIPT (all methodologies) and ultrasound can be due to a number of well documented reasons – including maternal transplant history. Here we discuss 11 select examples of fetal sex discrepancies and/or abnormally strong male results, which were later revealed to be due to a maternal transplant.

II. Methods

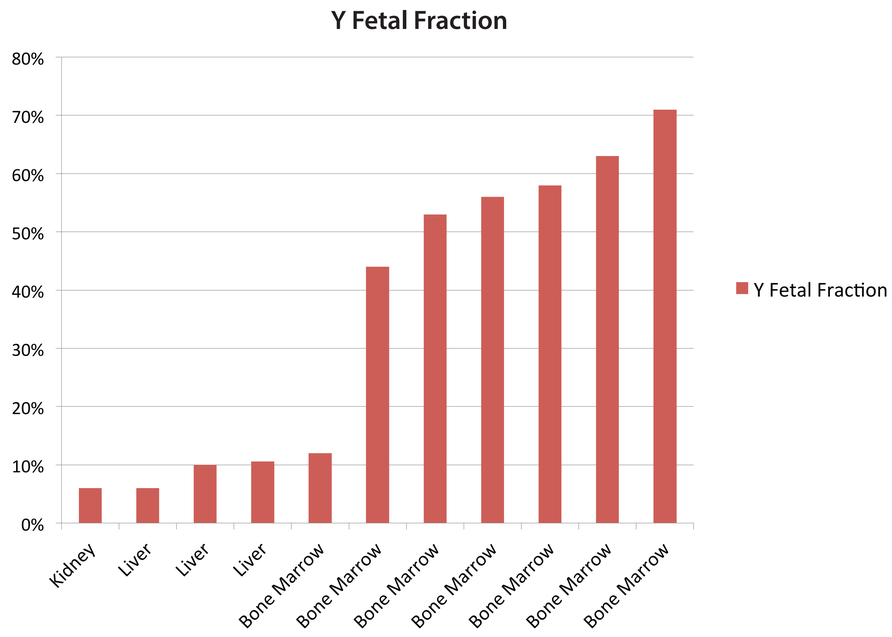
Maternal blood samples submitted to Sequenom Laboratories® for MaterniT®21 PLUS or MaterniT® GENOME testing were subjected to DNA extraction, library preparation, and genome-wide massively parallel sequencing as described by Jensen et al and Lefkowitz et al.[1,2]

III. Results

Table 1. Transplant type versus Y contribution

Case Number	Transplant Type	Fetal Fraction	Y Fetal Fraction	Z-score Y Chromosome	Test Ordered	Gender Discrepancy
1	Kidney	4%	6%	128	MaterniT21 PLUS	Unknown
2	Liver	8%	6%	144	MaterniT21 PLUS	Yes
3	Liver	8%	10%	203	MaterniT21 PLUS	Yes
4	Liver	8%	11%	203	MaterniT21 PLUS	Yes
5	Bone Marrow	8%	12%	299	MaterniT GENOME	Yes
6	Bone Marrow	10%	44%	720	MaterniT21 PLUS	Unknown
7	Bone Marrow	15%	53%	942	MaterniT21 PLUS	Unknown
8	Bone Marrow	10%	56%	6,468	MaterniT21 PLUS	Unknown
9	Bone Marrow	13%	58%	1,430	MaterniT GENOME	Yes
10	Bone Marrow	12%	63%	1,244	MaterniT21 PLUS	Unknown
11	Bone Marrow	10%	71%	1,388	MaterniT GENOME	No

Figure 1. Y Fetal Fraction by transplant type



IV. Conclusion

Fetal sex discrepancies between ultrasound and NIPT are a rare but known limitation of all NIPT methodologies. These discrepancies can be explained by a co-twin loss (or vanishing twin/second sac), fetal sex reversal syndromes/ chromosome abnormalities, maternal chromosome abnormalities, and history of transplant. Fetal sex discordance may not always prompt fetal or neonatal karyotyping, but it should be considered in certain circumstances. Data from this cohort suggests not all tissues/organs equally contribute cfDNA to maternal plasma and can mimic fetal data/placental contribution. Bone marrow transplants have a greater impact on Y fetal fraction than liver or kidney transplants in this small cohort. We would not expect the aneuploidy risk assessment to be adversely impacted by this transplant history, only fetal sex. Inquiring about history of maternal transplant is an important part of pre-test counseling and NIPT fetal sex interpretation. Prenatal screening requires a multifaceted approach to uncover the whole story.

V. References

1. Jensen TJ, Zwiefelhofer T, Tim RC, et al. High-throughput massively parallel sequencing for fetal aneuploidy detection from maternal plasma. *PLoS One*. 2013;8(3):e57381. doi:10.1371/ journal.pone.0057381. Epub 2013 Mar 6.
2. Lefkowitz RB, Tynan J, Liu T, et al. Clinical validation of a non-invasive prenatal test for genome-wide detection of fetal copy number variants. A*m J Obstet Gynecol*. doi: http://dx.doi. org/10.1016/j.ajog.2016.02.030.

LabCorp

Poster presented at the *NSGC Annual Conference*; 2018 November 14-17; Atlanta, GA.