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

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 cell-free DNA 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