EP04.28: Sex discordance following non-invasive prenatal screening
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BACKGROUND

With the increasing availability of non-invasive prenatal screening (NIPS) and high-resolution ultrasound, more cases of sex discordance are being identified in routine clinical practice. Knowledge about the limitations of NIPS and reasons for discordant results are critical for counseling parents. Here we present two cases from a single tertiary care referral center. We also review the literature to address potential causes of genotype-phenotype discordance.

METHODS

Permission to review medical records was approved by the Institutional Review Board at the University of Florida as an expedited review under a waiver of informed consent. Cases were identified using ICD-9 (January 1, 2013 – September 30, 2015; ICD-9-CM 752.2 "Indeterminate sex and pseudo-hermaphroditism") and ICD-10 codes (October 1, 2015 – January 30, 2019; ICD-10-CM Q56.4, "Indeterminate sex, unspecified") at UF Health. In addition, the departmental genetic counseling database and cytogenetics laboratory logbooks were reviewed to identify additional cases. When discordant results were suspected, the patients’ records were reviewed for maternal age, mode of conception, NIPS laboratory utilized, presence of multiple gestation, sonographic findings, subsequent prenatal or postnatal confirmatory test results, and pregnancy as well as neonatal outcomes. Data were collated upon review of all medical records describing NIPS results, prenatal care, postnatal care and clinical evaluation of mother and infant.

RESULTS

In our first case, a 37 year old P2012 underwent NIPS at 11 weeks gestation and monosomy X was identified. Morphological sonographic assessment at 20 weeks gestation was consistent with a female fetus following an amniocentesis at 16 weeks that revealed normal 46, XX karyotype. During the third trimester, the patient was diagnosed with stage IV invasive ductal carcinoma of the breast. Postnatal follow up of the neonate was consistent with a phenotypic female.

In the second case, a 22 year old P1001 obese female underwent NIPS at 14 weeks gestation and normal 46, XY karyotype was identified. Morphological sonographic assessment at 20 weeks was inconsistent with a male fetus. The patient declined invasive testing. The newborn was phenotypically female. Ultrasound of the neonate revealed uterus and karyotype resulted in a 46, XX male. Reason for discordant results was not identified.

CONCLUSIONS

These cases demonstrate the possible limitations of correctly identifying sex chromosomes via NIPS. Even with single nucleotide polymorphism based NIPS, positive predictive value for detection of sex chromosome abnormalities is around 50%. Invasive diagnostic procedure or postnatal genetics should be performed especially in case of sex chromosome discordance where NIPS may have subpar performance.

REFERENCES


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