10.5005/jp-journals-10028-1264

Staff Clinical Meeting

Contingency Screening using Noninvasive Prenatal Test for the Detection of Trisomy 21

Presenter: Japleen Kaur[1]
Moderator: Jasvinder Kalra[2]
Faculty: Rashmi Bagga[3], PK Saha[4], Rimpi Singla[5], Aashima Arora[6]

BACKGROUND

Screening for aneuploidies is a vital component of routine antenatal care. Conventional screening methods include biochemical screening and ultrasonography. Interpretation of these tests and further course of management can be enigmatic. Noninvasive prenatal test (NIPT) using cell-free fetal deoxyribonucleic acid (DNA) is an emerging screening method with accuracy close to the diagnostic invasive tests. We present a case of an elderly primigravida, conceived after years of infertility, in whom the first trimester combined screen was reported as intermediate risk and NIPT helped in reaching the diagnosis of fetal Down's syndrome.

CASE REPORT

A 39-year-old primigravida presented to our antenatal outpatient department at 9 weeks period of gestation (PoG) for routine antenatal visit. She had received treatment for primary infertility for 10 years, although index pregnancy was spontaneous conception. Fetal viability and dating had already been confirmed on early ultrasound at 8 weeks gestation. Routine antenatal investigations were advised. She was also advised regarding aneuploidy screening, with dual screen and ultrasound for nuchal translucency at 11 to 13 weeks. Her background risk for Down's syndrome (due to age >35 years) was 1:158. Her first trimester biochemical screen [beta-human chorionic gonadotrophin (hCG) and pregnancy-associated plasma protein A (PAPP-A)] showed a final risk of 1:111. Considering the nuchal translucency of 1.2 mm, combined risk of 1:729 was ascribed. Falling in the range of 1:100 and 1:1000, the report was interpreted as intermediate risk. The couple underwent genetic counseling and were explained the options. They could go for diagnostic invasive tests or further screening tests, which included noninvasive prenatal screening test or genetic sonogram and second trimester screening tests. Considering the risks of invasive testing and both the pros and cons of NIPT, the couple opted for NIPT. At 14 weeks PoG, maternal blood was sent for Panorama test (Medgenome Laboratories) for NIPT, which was conducted using the "next-generation aneuploidy test using single-nucleotide polymorphisms." Further, NIPT reported a high risk of Down's syndrome (>99/100). Follow-up counseling was done and confirmatory diagnostic test was advised. Patient underwent amniocentesis at 17 weeks. Fluorescent *in situ* hybridization and karyotype confirmed the presence of Trisomy of chromosome 21. She underwent medical termination of pregnancy at 20 weeks PoG, using standard protocol of mifepristone and misoprostol. A female fetus of 500 gm was delivered. Confirmatory testing on abortus could not be done citing financial reasons.

DISCUSSION

Aneuploidies contribute significantly to perinatal morbidity and childhood disability. Screening helps to allay parental anxiety and also decreases the number of invasive tests for this indication. Conventional methods of aneuploidy screening include first and second trimester biochemical screens and ultrasonography. First trimester combined screening, incorporating maternal age, serum-free beta-hCG and PAPP-A and nuchal translucency, has a detection rate of 85 to 90% for Trisomy 21, with a false positive rate of 5%.[1] While the detection rate from screening using newer methods like maternal cell-free fetal DNA is 99.3% (false positive rate: 0.1%), it is not yet recommended for routine primary screening owing to high cost.[2] Recent studies have evaluated the role of cell-free DNA as a part of contingent screening, wherein triaging is done based on the conventional first trimester

[1]Senior Resident, [2,3]Professor, [4]Associate Professor, [5,6]Assistant Professor

[1-6]Department of Obstetrics and Gynecology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Corresponding Author: Rashmi Bagga, Professor, Department of Obstetrics and Gynecology, Postgraduate Institute of Medical Education and Research, Chandigarh, India, Phone: +919872494602, e-mail: rashmibagga@gmail.com

screening and then cell-free DNA testing is advised for those with intermediate risk.[3] This approach balances the cost and the need for invasive testing, for maximum detection rate.[4] Our patient aged 39 years fell in the high-risk population. Her first trimester combined screen was reported as 1:729, i.e., intermediate risk. She had conceived after years of infertility and so the option of NIPT using cell-free DNA was most preferable compared with direct invasive testing *vs* following up with second trimester screen and genetic sonogram. The NIPT report of our patient suggested high risk of Trisomy 21. As it is only a screening test, confirmatory testing with invasive test is still recommended. Amniocentesis was done for our patient and karyotype confirmed Trisomy 21. Moreover, NIPT has its limitations. It is not advisable for low-risk population and multiple gestations at present, due to a small but definite risk of false positive.[5] In some cases, result may be uninterpretable (due to early gestation, maternal obesity leading to low fetal fraction or placental mosaicism). In such cases, diagnostic tests and ultrasound evaluation should be offered, although repeat sampling has also been considered.[6] Therefore, the role of pre- and posttest counseling for NIPT must be emphasized.

CONCLUSION

In the current scenario, the most cost-effective strategy for aneuploidy screening is combined first trimester screening in all women and offering contingent NIPT for those being categorized as intermediate risk. On an individual basis, option of upfront NIPT or invasive testing can be offered to women at high risk for aneuploidies, with proper counseling.

REFERENCES

1. Nicolaides KH. Screening for fetal aneuploidies at 11 to 13 weeks. Prenat Diagn 2011 Jan;31(1):7-15.
2. Taylor-Phillips S, Freeman K, Geppert J, Agbebiyi A, Uthman OA, Madan J, Clarke A, Quenby S, Clarke A. Accuracy of non-invasive prenatal testing using cell-free DNA for detection of Down, Edwards and Patau syndromes: a systematic review and meta-analysis. BMJ Open 2016 Jan;6(1):e010002.
3. Kagan KO, Wright D, Nicolaides KH. First-trimester contingent screening for trisomies 21, 18 and 13 by fetal nuchal translucency and ductus venosus flow and maternal blood cell-free DNA testing. Ultrasound Obstet Gynecol 2015 Jan;45(1):42-47.
4. Tan TY. Combined first trimester screen or noninvasive prenatal testing or both. Singapore Med J 2015 Jan;56(1):1-3.
5. Grömminger S, Yagmur E, Erkan S, Nagy S, Schöck U, Bonnet J, Smerdka P, Ehrich M, Wegner RD, Hofmann W, et al. Fetal aneuploidy detection by cell-free DNA sequencing for multiple pregnancies and quality issues with vanishing twins. J Clin Med 2014 Jun;3(3):679-692.
6. Revello R, Sarno L, Ispas A, Akolekar R, Nicolaides KH. Screening for trisomies by cell-free DNA testing of maternal blood: consequences of a failed result. Ultrasound Obstet Gynecol 2016 Jun;47(6):698-704.