International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2020; 4(6): 285-286
Received: 16-09-2020
Accepted: 23-10-2020

Abhay Kumar
Junior Resident, Department of Obstetrics and Gynecology, PGIMER, Chandigarh, Punjab, India

Avir Sarkar
Junior Resident, Department of Obstetrics and Gynecology, PGIMER, Chandigarh, Punjab, India

Manisha Meena
Assistant Professor, Department of Obstetrics and Gynecology, PGIMER, Chandigarh, Punjab, India

Corresponding Author:
Avir Sarkar
Junior Resident, Department of Obstetrics and Gynecology, PGIMER, Chandigarh, Punjab, India

Wolf-Hirschhorn syndrome diagnosed in a precious IVF pregnancy: Ethical and therapeutic dilemma from an obstetrician's perspective

Abhay Kumar, Avir Sarkar and Manisha Meena

DOI: https://doi.org/10.33545/gynae.2020.v4.i6e.767

Abstract
Wolf-Hirschhorn Syndrome (WHS) is a very rare chromosomal anomaly resulting in early onset severe fetal growth restrictions, micrognathia, cleft lip, cleft palate and intellectual delay. Diagnosis of such a non-lethal syndrome does not mandate medical termination of pregnancy (MTP), especially in a precious IVF pregnancy. However, strong couple desire for MTP cannot be denied considering the lifelong morbidity of the resultant baby. So, the diagnostic and therapeutic dilemmas pose a challenge to obstetrical fraternity when WHS is discovered at 18 weeks gestation in a pregnancy resulting from donor gamete *in vitro* fertilization conception. Finally, after a long discussion and counselling, parents insisted to go for medical termination of pregnancy.

Keywords: Wolf-hirschhorn syndrome, *in vitro* fertilization, MTP, amniocentesis

Introduction
As the emaciated healthcare system is attempting to break the tide of the novel coronavirus pandemic across the globe, non-emergency services including OPDs have been suspended in majority of the hospitals to divert resources for combatting emergency medical care during this deadly pandemic. Infertility treatments including assisted reproductive technologies (ART) have been totally crippled. Fate of thousands of infertile patients seems to hang by a fine thread. In this critical hour, if a precious *in vitro* fertilization (IVF) pregnancy results in a rare congenital malformation, medical fraternity is left in a dire dilemma. We hereby report a very rare case of Wolf-Hirschhorn Syndrome (WHS) detected in second trimester in a donor gamete IVF pregnancy. This a probably the first case in literature which reports therapeutic challenges to WHS diagnosed in a donor IVF pregnancy.

Case report
A 32-year-old primigravida presented to a tertiary care hospital at 18 weeks gestation with detailed anomaly scan showing cleft lip, cleft palate and severe fetal growth restriction. She had a married life of 5 years with history of primary infertility. Husband's semen analysis was suggestive of oligozoospermia with a total sperm count of 0.5millions/microL. Current pregnancy was a result of IVF with donor semen obtained from unknown donor through sperm bank.

It was a singleton conception with no complications in the first trimester. Advanced first trimester scan at 12 weeks showed a nuchal translucency of 1.1 mm. Nasal bone was visible. There was no evidence of tricuspid regurgitation or ductus venosus flow reversal. Serum biochemical markers like free beta-hCG and Placental associated plasma protein (PAPP-A) were within normal range. Detailed anomaly scan was done at 18 weeks gestation and findings are as mentioned above. Fetal echo done did not reveal any abnormality. Infective etiologies like maternal toxoplasma, rubella, cytomegalovirus and syphilis were ruled out. The couple was highly apprehensive about the growth retarded status of their fetus but there was no indication for medical termination of pregnancy (MTP).

The clinical situation imposed a great diagnostic and therapeutic dilemma to the obstetrical team. Hailing from an affluent socioeconomic class, the couple insisted on going for an invasive test despite it being a precious IVF pregnancy. An amniocentesis was done and amniotic fluid was sent for Fluorescent in situ hybridization (FISH) and karyotyping. QF-PCR analysis revealed no abnormality in chromosomes 13, 18, 21 and sex chromosomes.

However, on comparative genome hybridization (CGH), a partial deletion was noted in short arm of chromosome 4.

Following the diagnosis of this rare chromosomal disorder called WHS, the couple desired to go for MTP by medical method. The abortus was a female of 220 grams. Gross examination was suggestive of cleft lip, palate and minimal micrognathia. Parents were repeatedly counselled for an autopsy but they did not consent for the same. Post abortal period was uneventful.

Husband had been evaluated for oligozoospermia and cause seemed likely to be pituitary with decreased FSH and LH. With pulsatile gonadotropin therapy, his sperm counts rose to 1.5 millions/microL. We are planning for next conception through husband's sperm via Intra-cytoplasmic sperm injection (ICSI). Maternal karyotype was normal. Prenatal genetic testing prior to implantation in next pregnancy shall help to eliminate the risks of subsequent fetal malformations.

Discussion

Around 30 lakh couples seek infertility treatment in India every year, among whom, 5 lakh undergo IVF. During this COVID 19 era, infertility services have really suffered a lot. With the declaration of social lockdown in the subcontinent, delay of infertility services has caused unimaginable mental and emotional toll on couples keen to embrace parenthood. Moreover, during this crucial time, if a donor gamete IVF conception results in a rare and non-lethal congenital malformation like WHS, we are left in a complete dilemma.

WHS is characterized by fetal growth restriction and varying degrees of developmental delays. Most neonates have distinctive facial morphology in the form of high forehead, highly arched eyebrows, epicanthal folds, described as the "Greek warrior helmet" appearance. Additional features include a flat, broad nasal bridge, low-set ears, micrognathia, fish-like mouth, dental problems including missing teeth, cleft lip and cleft palate [1].

Although the reported incidence of WHS is estimated to be around 1:50,000 births, it is thought to remain undiagnosed in quite many. About 40-45% infants with WHS inherit a de novo simple deletion of 4p16.3 and other 45% have an unbalanced translocation with a combination of 4p deletion and a partial trisomy of a different chromosome arm (like chromosome 8) [2]. Heterozygous inversions on 4p16 and 8p23 were present in 12.5% and 2.5% were double-heterozygous. Larger deletions tend to result in more severe intellectual disability and physical abnormalities than smaller deletions [1]. Female fetuses are more commonly affected compared to males (2:1) [1, 2]. Midline defects including brain, palate, heart and genitalia are most lethal. Difficulty in ambulation arise due to characteristic ataxic gait and marked muscle hypotonia. Intellectual disability ranges from mild to severe. Though their socialization skills are strong yet, verbal, communication and language skills tend to be weaker.

Diagnosis includes history of early-onset severe fetal growth restriction, decreased fetal movements and placental insufficiency [3]. Although obstetric ultrasound suggesting typical microcephaly, micrognathia and "Greek warrior helmet" appearance is reported to be common in literature, yet index case did not have any of these. Definitive diagnosis was clinched after fetal karyotyping on amniocentesis. Fetal cells showed definite partial deletion of the short arm of chromosome 4. FISH and array CGH are other methods of establishing the diagnosis [4].

Neonates with WHS face multiple comorbidities and hence detailed evaluation and parental counselling is the need of the hour. Evaluation of cognitive, language, social and motor skills will indicate the child's developmental delays. Inability to suckle the nipples, feed intolerance and gastro-esophageal reflux can cause immediate neonatal emergency. Severe immunodeficiency predisposes to early onset sepsis. Abnormal renal and liver function tests are indirect evidences to structural renal anomalies and hepatic adenomas [5].

WHS does not mandate MTP. Parental counselling with detailed discussion regarding the neonatal and long-term outcomes in of utmost importance. Management strategy depends on a case-to-case basis. It is the joint decision of the treating obstetrician and the parents who mutually decide whether to terminate the pregnancy or continue it to term.

Conclusion

Chromosomal microarray technology, FISH and G-banded cytogenetic studies are necessary for complete characterization of WHS. Genetic counselling and prenatal diagnosis are of importance to determine the chromosomal status of subsequent pregnancies. Fetal aneuploidy screening and detailed anomaly scans shall help in timely detecting subtle markers of malformations. Invasive tests with resultant karyotyping is the only diagnostic tool for detecting syndromic associations. In this era of nanotechnology, PGT is thus becoming a major tool for prenatal aneuploidy screening in ART conceived pregnancies.

References

1. Pokale YS, Jadhav AM, Kate U. Wolf-Hirschhorn Syndrome: a case demonstrated by a cytogenetic study. Indian J Human Genetics 2012;18(1):1-3.
2. Rezai S, Wilansky J, Gottimukkala S *et al*. Wolf-Hirschhorn Syndrome (WHS), a case report and review of literature. J Pediatr Neonatal Care 2016;5(1):170-175.
3. Bulak H, Kopanska D. Wolf-Hirschhorn syndrome- a case report. Pediatr Med Rodz 2017;13(2):267-269.
4. Byeon S, Myung JK, Park SH. The Wolf-Hirschhorn Syndrome in fetal autopsy- a case report. The Korean J Pathol 2011;45(S1):S15-19.
5. Gamble JF, Kurian DJ, Udani AG *et al*. Airway management in a patient with Wolf-Hirschhorn Syndrome. Case Reports in Pediatrics 2016;23(2):485-489.