Medpress Journal of Gynecology and Obstetrics

Oocyte Donation and Surrogate Pregnancy-Fertility Options and Challenges, Possibilities and Opportunities for a Patient with Complete Androgen Insensitivity Syndrome

Neeva D. Govani[1], Dhaval R. Govani[1], Namrata G. Panchasara[1], Rasila R. Patel[1], Partap Kumar Midha[2], Ramnik V. Patel[1,*]

[1] Department of Pediatrics and Pediatric Surgery, Postgraduate Institute of Child Health & Research and KT Children Govt University Teaching Hospital, Rajkot 360001, Gujarat, India.

[2] J. Watumull Global Hospital & Research Centre, Delwara Road, Mount Abu, Rajasthan 307501, India affiliated to medical faculty of God fatherly spiritual university, Mount Abu, Rajasthan.

Case Report

***Corresponding author**

Ramnik V. Patel, Department of Pediatric Surgery, Postgraduate Institute of Child Health & Research and KT Children Government University Teaching Hospital, Rajkot, 360005, Gujarat, India. Mobile: 00447956896641, Fax: 00441162893395, E-mail: ramnik@doctors.org.uk.

Article Information

Received:15-03-2022;
Accepted: 22-04-2022;
Published: 31-05-2022.

Abstract

We wish to present a very unusual case of an interesting fertility in a known case of complete androgen insensitive syndrome. A 28-year-old female who developed bilateral inguinal hernias in childhood and underwent operation of bilateral inguinal herniotomy at which she was found to have surprise findings of having testes on both sides and the surgeon at that time realised that she was a case of complete androgen insensitive syndrome as she has blind ending vagina and no ovaries and uterus. The surgeon explained the parents that she needs removal of both gonads for cancer risk and repair of inguinal hernias which was successfully treated. While studying at college, she had love with one of his boyfriends and got married. Physical examination showed secondary sex characteristics well developed. The couple had consulted few fertility specialists but their hopes of having the baby was turned down and finally they approached our god fatherly spiritual university teaching hospitals at the fertility clinic. A thorough family pedigree and family history on both sides followed by reviewing all their investigations suggested possibility of having baby via a plan in which she gets an oocyte donation from her sister and the sister of the husband was very keen to provide surrogacy and father's sperm fertilisation will bring a baby to the lovely aspiring couple. The plan was implemented and a baby girl was delivered at term uneventfully.

Keywords: Androgen Insensitivity Syndrome, Assisted Reproduction Technology, Female Bilateral Inguinal Hernia, Infertility, Oocyte Donation, Surrogacy.

Introduction

The traditional definition of medicine has been described as art and science. With advent of information explosion, evidence-based medicine and wide spread application of advanced technology to the medical field led to modification of the definition to include triad of art, science and technology. However, despite the best available technology, some of the problems eluded the definition and recently the fourth dimension of spirituality has been added to complete it. Recent advances in assisted reproductive technology (ART), coupled with the emerging understanding in molecular mechanisms of disorders of sex development (DSD) and that of associated genetic infertility, have given hopes for fertility in groups of patients who till recently were denied biological parenthood. Those with partial androgen insensitive syndrome (PAIS) due to genetic mutation of androgen receptor have a spectrum of abnormality like hypospadias, micropenis, undescended testes and male infertility. Though 46xy PAIS males have possibility of fatherhood complete AIS patients are female phenotype and are raised as females.

Case Report:

An adult 28-year-old female primary school teacher who was born as apparently normal girl at term. Everything seemed normal till her early childhood when she developed bilateral inguinal hernias. She underwent operation of bilateral inguinal herniotomy at which she was found to have surprise findings of having testes on both sides and the surgeon at that time realised that she was a case of complete androgen insensitive syndrome as she has blind ending vagina and no ovaries and uterus. The surgeon explained the parents that she needs removal of both testes for associated cancer risk and repair of inguinal hernias with bilateral gonadectomies were successfully performed.

When she came to know that she has a genetic condition that means she has no reproductive organs and she remembered

Citation: Patel RV, Govani ND, Govani DR, et al; Oocyte Donation and Surrogate Pregnancy-Fertility Options and Challenges, Possibilities and Opportunities for a Patient with Complete Androgen Insensitivity Syndrome. Medp J Obstet Gynaecol. 2022; 1(1): mpog-202203001.

tearfully telling her younger sister of her sorrow that she would never be a mother. It was then that younger sister promised to donate one of her own eggs when the time came. Years later, married and desperate to start a family, she asked her little sister if she had really meant what she said. She was happy to donate but being unmarried reluctant to carry the baby for 9 months as first pregnancy. As an unmarried girl to have pregnancy in Indian culture was barely unacceptable rationally for her and emotionally, she was not prepared to hand over the first baby to her sister. Both parents were reluctant to find a stranger to act as a surrogate after hearing stories about women who demanded to keep the baby at the last minute.

Both parents always knew they wanted a baby of their own. But with wife unable to have children because of a rare genetic condition, they realised they might need some help to make their dream of a family come true. The couple had consulted few fertility specialists where her husband was found to be fertile but their hopes of having the baby was turned down. Finally, they approached our god fatherly spiritual university affiliated teaching hospitals at the fertility clinic to see if there was any hope in such complex case to have fertility by any means as the aspiring couple was very lovely with big joint families on both sides, Finally, when husband told his older sister, 32 years-old having two children, about the problem she offered to help so that genetically the baby will be a mixed of both parental side genetic materials.

She was otherwise healthy and did not have menarche or menstrual period as expected but was able to be sexually active and enjoy sex through her vagina. While studying at college, she had love with one of his boyfriends and got married. Her vital functions were within normal range. Physical examination showed secondary sex characteristics well developed but the clitoris and the labia were primitive. We noted the presence of surgical scars in her both groins with and prominent scar. Husband's physical examination was normal. Her blood test and urine laboratory tests including the husband's sperm analysis and hormone profiles were within normal limits. Her abdominal and transvaginal ultrasound examinations could not see both ovaries or the uterus as internal sexual organs.

A thorough family pedigree and family history on both sides followed by reviewing all their investigations by expert fertility specialists followed by a detailed discussion at a multidisciplinary meeting (MDT) of DSD. However, homologous fertility preservation using cryopreservation of either the mature oocytes following ovarian stimulation or that of ovarian tissue in prepubertal period before ovarian failure as in Turner syndrome for this group of patients seemed impossible. Heterologous fertility potentiation, in the cytogenetic infertility by donor oocytes, was a distinct possibility and has been successfully used by us. Single embryo-transfer and strict selection criteria and judicious use of this advanced technology were advocated by the MDT to minimize maternal morbidity and mortality.

However, MDT was of the opinion that with complete gonadal failure in her case, they need oocyte donation with intracytoplasmic sperm injection (ICSI)/ In vitro fertilization and embryo transfer (IVFET) for fertility. This category of patients is encouraged and known to resort to fertilization of donated oocyte using husband's sperms. Resultant embryos are transferred into surrogate uterus.

The parents carried a long search and started exploring the possibility of finding a surrogate stranger - but were put off by stories of some who dropped out or became too attached to the baby. Finally there sisters came to the rescue. In the end, that help came from close to home. husband's older sister, and wife's younger sister, joined forces to help them bring their baby into the world. Her sister was happy to provide the egg while sister-in-law was happy to carry the baby for nine months. All experts agreed to the suggested possibility of having baby via a plan in which she gets an oocyte donation from her sister and the sister-in law that is sister of the husband was very keen to provide surrogate pregnancy and father sperm will bring a baby to the lovely aspiring couple.

Pre-conception meeting was held with the patient, her husband and all their relatives on both sides and parents and their views and concerns were all explained and the detailed plan was given. So, the agreement was made. Wife's sister would provide the egg, Husband would fertilise it and it would be implanted into his sister, who would carry the baby. Over the next few months, husband's sperm was frozen, while his sister and sister-in-law were given hormone injections – one to build the lining of her womb and the other to help her produce more eggs to be harvested. Two embryos were implanted in his sister in December and she discovered she was pregnant on Christmas Eve. The 20-week scan revealed the family were expecting one baby, a girl. Pregnancy was monitored all through out which was uneventful and at term an apparently healthy 3200 grams weight full term baby girl was delivered via spontaneous vaginal delivery.

The post-delivery course of recovery was uneventful, and the patient, husband and families on both sides were very happy and satisfied with the fact that they could see the light at the end of the tunnel and that fertility is potentially possible even in a hopeless case of complete androgen insensitivity patients. Parent's dream has now come true and they are mother and father to the baby. Our case is an amazing example of use of art, science and assisted advanced reproductive technology with the sibling support from both parents and family affair of help and support made it possible eventually. If it wasn't for their sisters, they would still be childless and they felt that it's the best gift ever and they loved their sisters so much for it. Mother always knew she wanted to be a mother but it was just a question of how and husband can't believe that they are parents and felt like luckiest couple alive on this planet earth.

Discussion:

Advances in reproductive medicine in general and those in assisted reproductive technology in particular have revolutionized diagnosis of disorders of sex development and the management of the associated infertility. These advances have certainly provided fertility potentiation but require judicious application coupled with expert genetic counselling [1]. DSDs are a heterogeneous group of congenital conditions with variations in chromosomal, gonadal, or anatomical sex. Impaired gonadal development is central to the pathogenesis of the majority of DSDs and therefore a clear understanding of gonadal development is essential to comprehend the impacts of these disorders on the individual, including impacts on future fertility [2].

46, XY DSD can be caused by defects in androgen action, typically due to dysfunction of the androgen receptor (AR) [3]. DSD due to complete loss of function of the AR is called Complete Androgen Insensitivity Syndrome (CAIS), whereas mutations that retain some residual function result in Partial

Androgen Insensitivity Syndrome (PAIS). CAIS typically presents in adolescence as primary amenorrhea despite normal breast development. Alternatively, CAIS may present in childhood with palpable inguinal masses in an individual with a 46, XY karyotype and a typical female appearance to the external genitalia as has happened in our case. The phenotype in PAIS is variable depending on the degree of androgen sensitivity and there may be associated gynecomastia due to the peripheral conversion of testosterone to estradiol. Individuals with inactivating mutations of the LH receptor (Leydig cell hypoplasia) have a variable appearance ranging from a completely female phenotype to a variable degree of virilization, very similar to patients with AIS. However, breast development is not observed. Fertility is impaired in the majority of individuals with disorders of androgen action as a result of germ cell loss and/or failure of spermatogenesis [4].

DSD are defined as congenital conditions in which development of chromosomal, gonadal, or anatomic sex is atypical and a consensus statement has been issued that calls for patient- and family-centered care delivered by an integrated, interdisciplinary team [5]. The primary role of an integrated, interdisciplinary team would be to assess all of these perspectives and provide care that is founded on a patient- and family-centered model. Variability exists across stakeholder groups in the key concerns affecting young children/families with DSD. Interdisciplinary DSD healthcare team development should account for varying perspectives when counselling families and planning treatment [6].

Whereas the resulting recommendations for holistic, multidisciplinary care seem to have been implemented rapidly in specialized pediatric services around the world, adolescents often experience difficulties in finding access to expert adult care and gradually or abruptly cease medical follow-up. Many adults with a DSD have health-related questions that remain unanswered owing to a lack of evidence pertaining to the natural evolution of the various conditions in later life stages [7]. Our case is a living example of fertility problems later in her adult life.

Fertility potential in this population of DSDs is quite variable. Recent investigations into fertility potential in those previously thought to be infertile suggest that actually the majority may have fertility potential through experimental but evidence-based and experience-based protocols and the fertility preservation may be more in pediatric age groups. As fertility research and techniques advance, it is important to carefully consider pediatric ethical issues specific to this population, including gonadectomy, consent/assent, experimental treatment and false hope, cost and insurance coverage, genetic transmission to offspring, and gender dysphoria [8].

Gonadectomy is performed in our patient in childhood as it was thought at increased risk for germ cell cancer (GCC). The traditional clinical perception has long been that such gonads, without usual hormone function and fertility potential, lack purpose and that, given the GCC risk, should be removed. However, understanding of malignancy risk is evolving and GCC risk now can be stratified as in complete androgen insensitivity syndrome (CAIS) is <5%], whereas others confer intermediate or high risk such as partial AIS with cryptorchidism risk is ~50%). Accordingly, this risk stratification has allowed for timing of gonadectomy recommendations to be more individualized and recommend post pubertal gonadectomy or observation for patients with CAIS and strong consideration of prepubertal gonadectomy for those with partial androgen insensitivity syndrome [9]. GCC may take years to become invasive malignancy, which is generally localized and highly curable; thus, observation protocols may be reasonable for select individuals [10].

Conclusion

In conclusion, we believe that complete androgen insensitive sensitive syndrome is a very unusual and rare DSDs, and that it is almost impossible to have fertility until recently despite advances in art, science and technology in modern medicine due to the underlying genetic complexity of the case. We strongly believe in taking help of spiritual understanding and intervention and positive use of existing lovely relationships in a joint family with good communication and co-ordination in such cases. Expectations and choices also vary with cultural or parental expectations. Although extremely rare to have fertility in a case of CAIS, the parents and relatives were very happy and satisfied with the outcome. We believe that patients, parents, public, professionals and fertility experts, must still consider possibility of fertility as a possible outcome when encountering an adult couple with such a DSD.

Compliance with Ethical Standards

Conflict of Interest

The authors have no conflict of interest to declare. No funding source was involved in this study.

Ethical Approval

All procedures performed on human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from the parents and all the relatives involved prior to all the procedures. Parents and all involved parties were informed about the procedure.

References:

1. Vaidya, R.A., Gogte, J. Fertility options and challenges for patients with cytogenetic infertility & disorders of sex development. Mol Cytogenet 7, I20 (2014). https://doi.org/10.1186/1755-8166-7-S1-I20
2. Gomes NL, Chetty T, Jorgensen A, Mitchell RT. Disorders of Sex Development-Novel Regulators, Impacts on Fertility, and Options for Fertility Preservation. Int J Mol Sci. 2020 Mar 26;21(7):2282. doi: 10.3390/ijms21072282. PMID: 32224856; PMCID: PMC7178030.
3. Hughes I.A., Davies J.D., Bunch T.I., Pasterski V., Mastroyannopoulou K., MacDougall J. Androgen insensitivity syndrome. Lancet (Lond. Engl.) 2012; 380:1419–1428. doi: 10.1016/S0140-6736(12)60071-3.
4. Hannema S.E., Scott I.S., Rajpert-De Meyts E., Skakkebaek N.E., Coleman N., Hughes I.A. Testicular development in the complete androgen insensitivity syndrome. J. Pathol. 2006; 208:518–527. doi: 10.1002/path.1890.

5. Lee PA, Houk CP, Ahmed SF, Hughes IA in collaboration with the participants in the International Consensus Conference on Intersex. Consensus statement on management of intersex disorders. Pediatrics. 2006;118: e488–e500.
6. Kogan BA, Gardner M, Alpern AN, Cohen LM, Grimley MB, Quittner AL, Sandberg DE. Challenges of disorders of sex development: diverse perceptions across stakeholders. Horm Res Paediatr. 2012;78(1):40-6. doi: 10.1159/000339863. Epub 2012 Jul 20. PMID: 22832323; PMCID: PMC3478759.
7. Cools, M., Nordenström, A., Robeva, R. et al. Caring for individuals with a difference of sex development (DSD): a Consensus Statement. Nat Rev Endocrinol 14, 415–429 (2018). https://doi.org/10.1038/s41574-018-0010-8
8. Lisa Campo-Engelstein, Diane Chen, Arlene B. Baratz, Emilie K. Johnson, Courtney Finlayson, The Ethics of Fertility Preservation for Pediatric Patients With Differences (Disorders) of Sex Development, Journal of the Endocrine Society, Volume 1, Issue 6, 1 June 2017, Pages 638–645, https://doi.org/10.1210/js.2017-00110
9. van der Zwan YG, Biermann K, Wolffenbuttel KP, Cools M, Looijenga LH. Gonadal maldevelopment as risk factor for germ cell cancer: towards a clinical decision model. Eur Urol.2015;67(4):692–701
10. Albers P, Albrecht W, Algaba F, Bokemeyer C, Cohn-Cedermark G, Fizazi K, Horwich A, Laguna MP, Nicolai N, Oldenburg J; European Association of Urology. Guidelines on testicular cancer: 2015 update. Eur Urol. 2015;68(6):1054–1068.

Citation: Patel RV, Govani ND, Govani DR, et al; Oocyte Donation and Surrogate Pregnancy-Fertility Options and Challenges, Possibilities and Opportunities for a Patient with Complete Androgen Insensitivity Syndrome. Medp J Obstet Gynaecol. 2022; 1(1): mpog-202203001.