HIV Uninfected Conception in Serodiscordant Couple: Case Reports

Gynecology and Women's Health Care

Case Report

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Abstract

With the advances in assisted reproductive techniques, there are various methods to decrease the risk of HIV viral transmission by separating out uninfected sperm cells from viral reservoirs known to exist within the semen. We report two successful pregnancies in HIV-serodiscordant couples by using assisted reproductive technique i.e in vitro fertilization (IVF).

Introduction

Human immunodeficiency virus (HIV) infection which was earlier thought to be a terminal condition, now approached as a chronic illness with emphasis on improving the quality of life of patients due to the introduction of Antiretroviral therapy. It has greatly reduced the morbidity and mortality associated with the virus. In India, between 2000 and 2015, new HIV infections dropped from 2.51 lakhs to 86 thousand, a reduction of 66% against a global average of 35% [1]. As a consequence of therapeutic advances, many HIV-infected individuals want to have children now [2].

With the advances in assisted reproductive techniques, there are various methods to decrease the risk of HIV viral transmission by separating out uninfected sperm cells from viral reservoirs known to exist within the semen [3]. We report two such cases.

Case Report 1

A 37 years old female came to our Fertility Centre with primary infertility. Her hormonal profile showed – AMH: 1.8 ng/ml, FSH: 8.9 IU/ml, LH: 3.7 mIU/L, estradiol: 35 pg/ml, prolactin: 9.1 ng/ml, thyroid stimulating hormone: 2.3 pg/ml. Ultrasound showed normal ovaries and uterus. The husband's semen analysis showed azoospermia with normal hormonal profile and positive test for HIV infection. His viral load was undetectable (HIV RNA – less than 50 copies/ml) after taking anti retroviral therapy. The couple had previous history of one failed IVF cycle elsewhere.

In view of the above diagnosis, we recommended testicular biopsy and IVF ICSI to the couple. We used the antagonist protocol for ovarian stimulation. We stimulated the ovaries of patient with highly purified menotrophin HMG 450 IU (hpHMG, Menopur; Ferring GmbH, Germany). After six days of stimulation, transvaginal scan showed 4 good follicles of 14mm size in both ovaries. After that daily subcutaneous injection of GnRH antagonist, 0.25 mg Cetrorelix (Cetrotide, Merck Serono S.p.A, Italy), was added. When follicles reached 18 mm, 500 mcg recombinant hCG (rhCG, Ovitrelle; Merck Serono S.p.A, Italy) was given to trigger ovulation.

With all universal precautions, transvaginal oocyte aspiration of ovaries was performed before 36 h, under ultrasound guidance, using Wallace OPU needle and we retrieved 3 oocytes.

The eggs were screened and counted under the stereozoom microscope by the embryologist. They were collected in the center well dish containing the Cook gamete buffer (a specially designed HEPES buffer meant that maintains pH in atmospheric CO2). Post egg collection, the eggs were transferred to the Cook fertilization media which is a bi-carbonate buffered medium.

On the day of egg pick up, the fact that the male partner was azoospermic, warranted testicular biopsy. The biopsied tubules were checked by the embryologist for the presence of sperm by teasing the tissue with 1ml BD falcon needle in Cook gamete buffer media. After ascertaining the presence of sperm, the fluid was then washed by double layer density gradient method (Puresperm Grad II sperm processing kit), for 15min at 2000 rpm.

The supernatant was discarded and the pellet was again washed with Cook gamete buffer media for 10 min at 2000 rpm. The supernatant was discarded and the resulting pellet was overlaid with 20 microlitres of Cook gamete buffer.

The oocytes were denuded in the Sage Hyaluronidase medium(80 IU/ml), followed by gamete buffer, for cumulus removal before the ICSI process. The maturity of the eggs was assessed. The sperm and oocytes were then respectively transferred to the ICSI dish containing the sage Poly Vinyl Pyrrolidone (PVP) droplet for sperm immobilization; and Cook gamete buffer droplets for oocyte injection and the ICSI procedure was then performed under the inverted microscope at 40X magnification.

After the ICSI procedure the fertilized eggs were then cultured in the Cook cleavage medium for specific development of zygotes, overlaid with mineral oil, for 2 days. One good embryo (grade A) was formed which was transferred via cook Sydney IVF catheter on day 2.

Progesterone suppositories 200 mg (Naturogest, Zydus Cadila Healthcare Ltd., German Remedies) twice daily was started from the oocyte retrieval day of the patient. After 14 days of luteal support, beta HCG was done which came positive. Ultrasound was done after two weeks of beta HCG that showed intrauterine single live pregnancy of six weeks. Antenatal period was uneventful and she delivered a HIV uninfected male baby of 3.1 kg.

Case Report 2

In second case report, a 32 years old female came to our Fertility Centre with primary infertility. Her hormonal profile showed – AMH: 4.6 ng/ml, FSH: 6.9 IU/ml, LH: 4.7 mIU/L, estradiol: 39 pg/ml, prolactin: 15.3 ng/ml, thyroid stimulating hormone: 1.5 pg/ml. Ultrasound showed normal ovaries and uterus. The husband's semen analysis showed low sperm count of 5 million/ml with progressive motility of 15% and the positive test for HIV infection. His viral load was undetectable (HIV RNA – less than 50 copies/ml) after taking anti retroviral therapy.

In view of the above diagnosis, we recommended IVF ICSI to the couple. We used the antagonist protocol for ovarian stimulation and stimulated the ovaries with the recombinant human FSH 180 IU (rhFSH, Folisuge; Intas Pharmaceuticals Ltd, India). After six days of stimulation, transvaginal scan showed 10 good follicles of 14mm size in both ovaries. After that daily subcutaneous injection of GnRH antagonist, 0.25 mg Cetrorelix (Cetrotide, Merck Serono S.p.A, Italy), was added. When follicles reached 18 mm, 500 mcg recombinant hCG (rhCG, Ovitrelle; Merck Serono S.p.A, Italy) was given to trigger ovulation.

With all universal precautions, transvaginal oocyte aspiration of ovaries was performed before 36 h, under ultrasound guidance; using Wallace OPU needle and we retrieved 10 oocytes.

On the day of egg pick up, the husband gave the semen sample that was washed by double layer density gradient method followed by Swim up method.

The fertilization was done by ICSI procedure. Eight good embryos (grade A) were formed out of which three embryos were transferred via cook Sydney IVF catheter and five embryos were frozen in two vials on day 2. After 14 days of luteal support, beta HCG was done which came positive. Ultrasound was done after two weeks of beta HCG that showed intrauterine single live pregnancy of six weeks. Antenatal period is uneventful till date.

Discussion

With the introduction of antiretroviral therapies, life expectancy of seropositive patients as well as their quality of life has dramatically improved during the last 10 years, and many couples with an HIV-positive partner can consider pregnancy planning [4].

In serodiscordant couples in which the male partner is infected, assisted reproductive technology (ART) is the safest way to prevent sexual transmission. Different methods of semen washing such as density gradient swim up or combination methods followed by simple wash were used to wash the sperms in various studies to reduce the transmission of HIV [5-7]. Spermatozoa are isolated by sequential density gradient and swim-up techniques and are subsequently tested by PCR assays for the presence of HIV RNA [8]. In our case, we also used density gradient technique followed by swim up method. Sperm washing eliminates round cells, seminal plasma, and the majority of immotile sperm. After the sperm-washing procedure, there are two main options to achieve a pregnancy: intrauterine insemination (IUI) and in vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI). In couples with a normal fertility evaluation, IUI is an effective approach. If semen analysis is abnormal, then IVF/ICSI is undoubtedly the treatment to be offered [9,10].

Assisted reproduction clinics handling infected cases like HIV should follow the safety guidelines for good laboratory practice. ART laboratory personnel should be trained to "treat each sample as potentially infectious" and "to ensure aseptic conditions for gametes, zygotes and embryos". Simple laboratory organizational precautions include uncluttered work surfaces, phasing out of sharp-edged glass items, no mouth pipetting, hygienic working conditions (procedures using appropriate equipment and disposables), regular cleaning and decontamination of the laboratory (quality control measures), proper (hazardous) waste disposal and strict access control to different laboratory sections. On a personal level, skin breaks should be protected with waterproof dressings and non-toxic powder-free gloves should be worn at all times, together with appropriate attire (barrier precautions - clothing, masks, gowns, and goggles). Biosafety for ART procedures are classified as level 2, with supplementary precautions when processing HIV samples. Specimens from infected patients should be processed, cryopreserved and stored in dedicated areas using separate storage tanks with adherence to specific safety measures. Seropositive patients can alternatively be batched or scheduled to allow sufficient decontamination of the laboratory after contact with patient's body fluids, i.e. semen processing, follicular fluid- aspirations and embryo transfer. All procedures and manipulations that can produce aerosols or splatter should be performed in Class II biological safety cabinets (BSCs) with vertical laminar flow, using aseptic techniques and sterile disposables. The use of a single-step embryo culture system should also minimize manipulations and exposure to unfavourable conditions outside of the incubator. In addition, microdroplet cultures under oil should speedup embryo evaluation and protect the culture medium from environmental contaminants when only

large upright incubators are available; and/or air filtration or a positive pressure system is not available [11].

Now as we know ART reduces the risk of contamination of the uninfected partner and helps couples to conceive, but preconception counseling is highly recommended among HIV serodiscordant and seroconcordant couples, allowing them to make more informed choices in order to reduce sexual transmission and improving pregnancy outcome.

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