

Successful Treatment of Testicular Failure Type IV Without Micro-Testicular Epididymal Sperm Extraction: A Case Report

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Abstract

Objective: Sperm donation and hormonal therapy with micro-Testicular Epididymal Sperm Extraction (TESE) for infertility from testicular failure might not always be available in some contexts. We report a successful embryo transfer from the patient-by 'cumulative sperm collection' strategy.

Case report: A 42 year-old male presented with non-obstructive azoospermia from testicular failure. Hormonal treatments were given along with the patient-initiated 'cumulative sperm collection' strategy, which eventually resulted in 17 sperms retrieved. Twelve mature oocytes were selected for intracytoplasmic sperm injection (ICSI) with the retrieved sperms, of which 8 oocytes were successfully fertilized but only two reached the early blastocyst stage; the first embryo transfer was not successful. Another five eggs were thawed and fertilized with the remaining 5 sperms and 3 oocytes were successfully fertilized: Seven cells were grade 3, 6 cells were grade 3, and 3 cells were grade 3. The second embryo transfer was successful, and the term female infant was successfully delivered by cesarean section.

Conclusion: At a center without micro-TESE availability, successful embryo transfer for testicular failure type IV could be achieved by hormonal therapy plus a 'cumulative sperm collection' strategy.

Keywords: Azoospermia; Hypogonadism; Sperm Retrieval

Introduction

Non-obstructive azoospermia (NOA) defined as no sperm in the ejaculated semen could be from inadequate gonadotropin production (hypogonadotropic hypogonadism) or intrinsic testicular impairment (testicular failure). While the former is commonly treated with hormonal therapy,

spermatogenesis in a majority of testicular failure cases has been believed to be untreatable and usually ended up with sperm donation (1-3).

Testicular Epididymal Sperm Extraction (TESE) is a conventional surgery to retrieve the sperms inside the testis (if there are any). The technique has been improved by performing microscopically-TESE (Micro-TESE) that is available at a few institutions (4). Micro-TESE has been performed along with hCG-based hormonal therapy for testicular failure

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type 1 (hypospermatogenesis) and 2 (late maturation arrest), whereas FSH-based hormonal therapy for type 3 (early maturation arrest) has been under development and only sperm donation is offered for type 4 (Sertoli cell only).

Findings from recent studies suggested that hormonal therapy might stimulate spermatogenesis and increase sperm retrieval yield (1-3, 5, 6). In centers without micro-TESE availability, hormonal therapy is given to stimulate spermatogenesis in some cases before the sperm is retrieved by conventional TESE. The number of attempts is usually jointly determined by the clinician and the patient on a case-by-case basis.

Given a small number of sperm from each retrieval procedure, a testicular failure type IV patient proposed an idea to continue the hormonal therapy and collect the sperms until the cumulative number of sperm retrieved is satisfactory for the fertilization. As the purpose of sperm cryopreservation was to keep the sperm for future use, we applied this technique to keep each small number of sperms from each collection to have as many sperms as possible for the sperm selection process. The successful embryo transfer for this testicular failure type IV patient achieved by hormonal therapy plus 'cumulative sperm collection' strategy is presented here.

Case report

A 42-year-old Caucasian man came with primary infertility in September 2017. He worked at the U.S. Embassy in Myanmar. He was a regular good-looking muscular American man (height 187.4 cm, weight 93.2 kg, and body mass index 26.5 kg/m²). The patient had a history of testicular torsion and underwent surgery when he was 10 years old. At the urology clinic, only left varicocele was identified from the physical examination, which was confirmed by testicular ultrasonography. The semen analysis was performed and found no sperm. His blood levels of the follicular stimulating hormone (FSH), luteinizing hormone (LH), and total testosterone was 19.20 mIU/mL, 7.51 mIU/mL, and 4.34 ng/mL respectively whereas prolactin was 17.25 ng/mL and prostate-specific antigen (PSA) was 0.6 ng/mL. He was appointed for a varicocelectomy and referred to the infertility clinic. He was diagnosed with NOA and genetic analysis was performed. TESE was planned for histological diagnosis and possible sperm collection.

His wife was a 37-year-old Vietnamese housewife. Her menstrual cycle was regular with no

dysmenorrhea. Her infectious disease screenings before IVF were negative. Pelvic ultrasound revealed a normal uterus and both ovaries. On the 2nd day of her cycle, FSH was 3.6 mid/mL, estradiol 22.3 pg/mL. She was using IVF stimulation - antagonist protocol.

On September 12, 2017, his genetic analysis revealed a normal 46XY karyotype without Y microdeletion. TESE revealed nearly complete atrophic seminiferous tubules with fibrosis (Figure 1). On September 30, 2017, he underwent the surgery for high ligation of the left varicocele as planned.

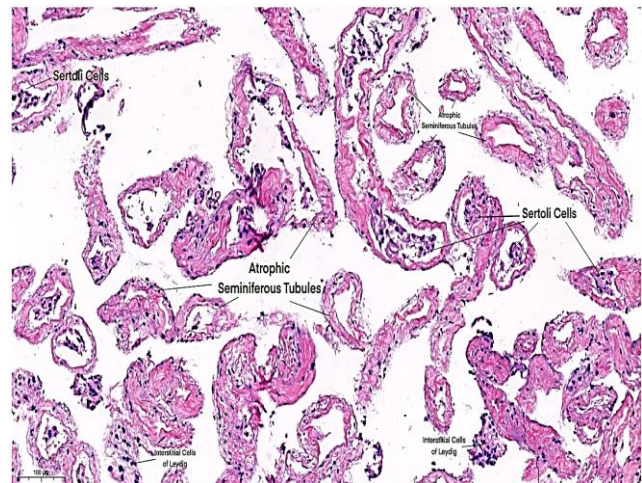


Figure 1: First TESE (before treatment) reveals the atrophic change of seminiferous tubule with fibrotic and hyaline change; some clusters of interstitial cells of Leydig are present; no sperms were identified.

In December 2017, he concurred with hormonal treatment with 2500 units of human chorionic gonadotropin (hCG, Pregnyl[®]) three times a week. In February 2018, his FSH became 2.20 mIU/mL, LH was 2.40 mIU/mL, and total testosterone was 3.87 ng/mL. Sperm analysis found 4 motile sperms. He reported improved libido; his sexual intercourse increased from one to eight times per month.

In April 2018, his anxiety was alleviated given the perceived sexual interest and activity. His FSH was 0.10 mIU/mL, LH was less than 0.10 mIU/mL, and total testosterone was 7.07 ng/mL. Sperm analysis revealed 106 sperms with 21 motile ones. After a lengthy discussion, the patient decided to pursue the hCG injection at the same dose and another TESE was planned. The second TESE was performed on May 4 to collect sperm but found only Sertoli cells without spermatogenesis (Figure 2). Nonetheless, the patient insisted to continue the hCG injection for another 2 months.

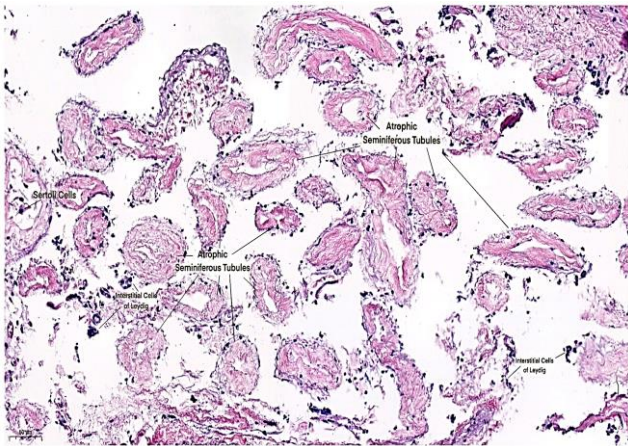


Figure 2: second TESE (after treatment) reveals the atrophic change of seminiferous tubule with fibrotic and hyaline change; some clusters of interstitial cells of Leydig are present; no sperms were identified.

In July 2018, his FSH was 3.00 mIU/mL, LH 0.50 mIU/mL, and total testosterone as 4.80 ng/mL (free testosterone 1.87%). Semen analysis revealed only 3-4 motile sperms. Nonetheless, the patient insisted to continue the hCG injection for another 2 months. The patient proposed a ‘cumulative sperm collection’ strategy—sperm collection every other 2 days until the total satisfactory amount is achieved. The chronological number of sperms retrieved were as follow: August 27 (8/slide), 31 (3/slide), September 6 (2/slide), 8 (2/slide), 29 (2/slide).

The ovarian stimulation was initiated on August 23 and oocyte retrieval performed on September 3 yielded 29 oocytes including 24 mature oocytes. Twelve mature oocytes were selected for intracytoplasmic sperm injection (ICSI) with 12 of the 17 sperms retrieved. Eight oocytes were successfully fertilized but only two reached the early blastocyst stage. The first embryo transfer was done on September 30 but the B-hCG level was not elevated on the ninth day. On October 26, another five eggs were thawed and fertilized with the remaining five sperms. Three oocytes were successfully fertilized: (1) 7 cells grade 3, (2) 6 cells grade 3, and (3) 3 cells grade 3. The first two were used for the second embryo transfer on October 10 (Figure 3).

The couple went back to Myanmar and got the first b-hCG on November 12 to be 160 mIU/mL. Antenatal care was promptly started with good compliance. The term female infant was successfully delivered by cesarean section in a hospital in the United States in July 2019.

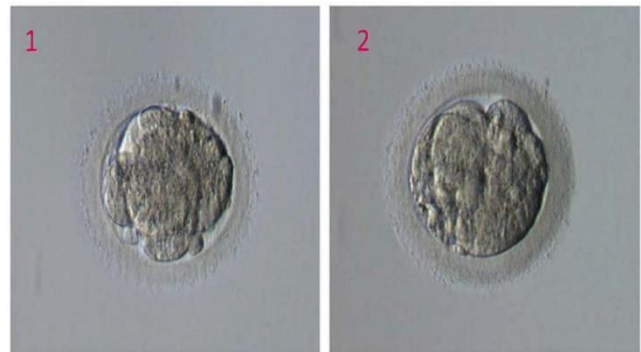


Figure 3: Successful Embryos

Discussion

Our case is the first to report the successful live birth in testicular failure type 4 (Sertoli cell only) by hormonal therapy to stimulate ejaculated sperms to be cumulatively collected so that they were adequate for the ICSI procedure at an institution with no micro-TESE availability.

Hormonal therapy with hCG has been used for type 1 (hypospermatogenesis) and type 2 (late maturation arrest) in adjunction with micro-TESE whereas FSH-based hormonal therapy for type 3 (early maturation arrest) has been under development (6). As no further treatment is recommended for type 4 because of the extremely low sperm retrieval rate (6), sperm donation has been the primary option and hormonal therapy with micro-TESE (1-3) has been the secondary alternative. Stem cell therapy for spermatogenesis is a promising solution but still under development (2).

The nearly complete atrophic seminiferous tubules with fibrosis in the first TESE correlated to at least testicular failure type 3 so the hormonal therapy with micro-TESE should have been attempted. Unfortunately, the micro-TESE has not been available in Thailand, including our institution. A recent literature review on surgical sperm retrieval in NOA did not differentiate a special context in which micro-TESE is not available (4). Also, the seminiferous tubule hyalinization was not mentioned in the review, suggesting a poor prognosis of sperm retrieval (6).

An ethical dilemma was that the couple could have been referred to get the micro-TESE performed at another institution in other countries as infertility is not an urgent medical condition. Nonetheless, the hormonal levels and the patient’s sexual wellbeing were improving during the follow-up. Very few sperms were found in the ejaculated semen

suggesting that some testicular tissues have been responsive to the hormonal therapy. Without micro-TESE, we had to assume that some small parts of the testis might still be functional but have not yet been revealed with the conventional TESE. Hence, the hCG injection was continued and the second TESE was attempted but no sperms were identified. Nonetheless, the patient's strong intention to have his child resulted in an idea to accumulate the ejaculated sperms to achieve an adequate number of sperms for the ICSI procedure. There were no standard recommendations from the American Society of Reproductive Medicine (ASRM) and the European Society of Reproductive Medicine (7) about the lowest numbers of ejaculated sperms that can undergo the ICSI process (7), resulted in another ethical dilemma for testicular failure treatment. Our case provides evidence of using only 17 sperms from ejaculated semen for a successful ICSI.

Conclusion

Hormonal therapy is an essential adjunctive treatment for testicular failure. Fertility is possible if some testicular tissues are responsive and able to produce a few ejaculated sperms even without micro-TESE availability. 'Cumulative sperm collection' could be part of the treatment plan discussed with the patient.

Conflict of Interests

Authors have no conflict of interests.

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