CASE REPORT

Successful combination of transrectal electroejaculation and intracytoplasmic sperm injection in the treatment of anejaculation

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We describe the case of a couple whose infertility was caused by the absence of seminal emission following retroperitoneal surgery for testicular cancer. Ejaculate could be retrieved from the husband by rectal probe electroejaculation (RPE) but sperm quality was so poor that conventional in-vitro fertilization was impossible. With intracytoplasmic sperm injection of spermatozoa retrieved by RPE — a combination not reported previously — we were able to induce a pregnancy with successful outcome.

Key words: electroejaculation/intracytoplasmic sperm injection/loss of ejaculation

Introduction

Although in general the loss of ejaculation is a rare condition, accounting for ~2% of the population of a male infertility clinic (Hargreave et al., 1983), its incidence is higher in some groups of young adults of reproductive age. About 85% of spinal cord-injured men lose their ejaculations (Higgins, 1979). With supraselective nerve sparing operation techniques, the incidence of postoperative anejaculation is decreasing rapidly (Donohue et al., 1993), but still currently 10–15% of men who previously underwent retroperitoneal lymph node dissection (RPLND) in the treatment of their testicular cancer have lost the first phase of their ejaculation, the emission of spermatozoa into the prostatic urethra (Winfield and Lange, 1987). Other less frequent causes of loss of seminal emission are diabetes, extensive pelvic surgery or multiple sclerosis. In all these conditions, as far as retrograde ejaculation into the bladder can be ruled out, the absence of seminal emission is caused by injury of the adrenergic neural control of the ejaculatory organs. Furthermore, primary or psychogenic anejaculation without an organic disturbance has been described. Diagnosis and treatment options for these conditions are described elsewhere (Denil et al., 1992a).

Rectal probe electroejaculation (RPE) is an established treatment of genuine neurogenic loss of seminal emission following radical RPLND not responding to drug treatment (Ohl et al., 1991). Retrieval of the spermatozoa for assisted reproduction has to be performed under anaesthesia but is usually a short uncomplicated procedure. However, sperm quality is often low because of the underlying disease or because of the effects of chemotherapy which may destroy the germinal epithelium in the remaining testicle. We previously described that sperm cells retrieved with RPE not only demonstrate low motility and normal morphology, but also have substantial functional deficits (Denil et al., 1992b). Therefore, pregnancy rates remain low. Sometimes couples had to be discouraged from further treatment cycles because of extremely poor sperm quality.

The direct injection of a viable sperm cell into the cytoplasm of an oocyte [intracytoplasmic sperm injection (ICSI)] is considered a breakthrough in the treatment of male factor subfertility and opens possibilities of parenthood to couples formerly regarded as infertile. It offers pregnancy rates superior to those of conventional in-vitro fertilization (IVF) and can be performed with very low numbers of viable spermatozoa (Palermo et al., 1992; Van Steirteghem et al., 1993).

Case report

A 34 year old man had been diagnosed with left side testicular cancer at the age of 25 years. His testicle was removed and upon histological examination it revealed a non-seminomatous germ cell tumour (teratocarcinoma; pT3, pN0, M1; clinical stage II B). He underwent a radical RPLND in March 1986, followed by four courses of chemotherapy. This therapy resulted in a permanent complete remission.

After the RPLND, the patient observed no more antegrade ejaculations, although erections and orgasms were present. He subsequently married and wanted to conceive children. Donor insemination and adoption were discussed with the couple but not accepted.

A biopsy from the remaining testicle, performed 2 years prior to presentation, showed a quantitative reduction of spermatogenesis, albeit with complete maturation of the sperm cells. Retrograde ejaculation was ruled out and therapy with α-sympathetic drugs failed to restore his ejaculation. Serum concentrations of luteinizing hormone, follicle stimulating hormone and testosterone were normal, and scrotal ultrasound examinations demonstrated a homogeneous testicular parenchyma and a testicular volume of ~15 ml.

Transrectal electrostimulation was proposed to retrieve spermatozoa for assisted reproduction. We applied low current electrical energy with a Model 12 Seager Electroejaculator
We could induce an antegrade and a retrograde ejaculate without problems. However, the quality of the ejaculates was low: average concentration of $23 \times 10^6$ spermatozoa/ml and motility of category b (World Health Organization, 1992) of only 5%; 87% of the sperm cells had an abnormal morphology. A second transrectal electroejaculation did not show any improvement in this low quality.

The patient's wife was evaluated gynaecologically. The history of the 29 year old woman did not show any gynaecological disorders. She had had normal menstrual cycles of 28 days with ovulations on day 14. She had never been operated on and did not demonstrate any signs of endometriosis or pelvic inflammatory disease. Laparoscopy or tuboscopy was not performed. In addition, the endocrine parameters did not reveal any abnormalities.

A first attempt at intruterine insemination (IUI) in a non-stimulated cycle was scheduled. Again we were able to produce an ejaculate without difficulty but, following washing and separation of motile spermatozoa by the Percoll method, sperm quality was so poor that IUI could not be performed. A second attempt, with preparation of the wife for IVF, again failed because of an extremely low sperm quality after sperm separation, far less than the suggested limit of 200 000 motile spermatozoa in the prepared sample (Hultling et al., 1995). Nevertheless, in every sample a few motile sperm cells with moderate progressive motility were seen.

With the advent of the direct intracytoplasmic injection of single sperm cells into the oocyte, a new method could be offered to this couple. For the ICSI procedure, ovarian stimulation was achieved by the administration of human menopausal gonadotrophin (HMG) after pituitary suppression with a gonadotrophin-releasing hormone agonist (Decapeptyl Depot; Ferring, Germany) according to the long protocol. A total of 45 ampoules of HMG were given before ovulation induction by the administration of 10 000 IU human chorionic gonadotrophin (HCG) on day 16 of the treatment cycle. At the time of ovulation induction the leading follicle size was measured as 22 mm in diameter and the oestradiol concentration was 3257 pg/ml. At 36 h after ovulation induction, a vaginal ultrasound-guided puncture of the follicles for oocyte retrieval was carried out under general anaesthesia. In all, 12 oocytes were aspirated. The subsequent RPE session induced an antegrade ejaculate of 1.0 ml with a concentration of $10 \times 10^6$ spermatozoa/ml and a motility of 5% of categories a and b; none of the motile spermatozoa showed a normal morphology. The retrograde sample had a volume of 20 ml with $20 \times 10^6$ spermatozoa/ml and 10% motility of category b; no sperm cells had a normal morphology. Preparation of the spermatozoa for the ICSI procedure was carried out using the mini-swim-up method according to Al-Hasani et al. (1995). The whole ejaculate was centrifuged at 500 g in a 5 ml Falcon tube for 2 min and then resuspended in 0.5 ml Ham's F-10 medium with 10% umbilical cord serum. After transfer of the preparation into an Eppendorf tube, a second and third ultracentrifugation was performed similarly for 2 min at 500 g. Following these steps, the supernatant was removed and the pellet was coated with 10–20 μl of medium. Immediately prior to the ICSI procedure, 5 μl 10% polyvinylpyrrolidone solution were added to 1 μl of the sperm-containing droplet to reduce sperm motility (Al-Hasani et al., 1995). The oocytes were treated with 0.5% hyaluronidase for 30 s for enzymatic removal of the cumulus oophorus cells. Under stereomicroscopic guidance at a magnification of ×50, the cells of the corona radiata were removed mechanically with the aid of a Pasteur pipette. Subsequently the maturity of the oocytes was determined. Only metaphase II oocytes were used for ICSI. In our case, 10 such oocytes were treated by ICSI. Two metaphase I oocytes were not injected. At 18 h after injection, six out of the 10 oocytes showed signs of fertilization. After 48 h, three oocytes had cleaved to excellent 4-cell stage embryos. The remaining three fertilized oocytes had degenerated.

At 3 weeks after embryo transfer a pregnancy was confirmed by ultrasound and normally increasing serum concentrations of HCG. After an uneventful gestation of 40 weeks, a healthy girl was born and is developing normally.

**Discussion**

The loss of seminal emission was a common complication of bilateral radical RPLND. Thanks to the current supraselective nerve-sparing techniques for low stage disease, its incidence is diminishing rapidly. Nevertheless, still ~15% of men who underwent RPLND may present with neurogenic anejaculation. With RPE we are able to induce a sperm sample for artificial insemination in almost all of these patients. With IUI, up to 36% pregnancy rates can be reached (Ohl et al., 1991). If the sperm sample induced by RPE is of poor quality but still has a sufficient number of motile and normal sperm cells, conventional IVF can be successful (Hultling et al., 1995). However, patients treated by that centre had far better sperm motility and morphology characteristics than our patient.

The quality of ejaculates induced by RPE is invariably low. The sperm motility averages only 11%, and several biochemical and functional defects have been described (Hirsch et al., 1991; Denil et al., 1992b). Different factors in both the method of RPE and the underlying disease have been postulated to be responsible for this low quality, but none is proved. It is known, however, that 37–66% of testicular cancer patients are infertile at the time of diagnosis (Lange et al., 1987), and that one-third of the treated men suffer irreparable damage of the germinal epithelium of the remaining testicle by chemotherapy (Fossa, 1985). In our case, the quality of the retrieved spermatozoa was extremely poor despite a favourable biopsy 2 years earlier. The case is typical of some of our anejaculatory patients with extremely poor sperm quality at RPE, in whom even IVF does not lead to pregnancy of their wives or in whom the sperm quality is too low for conventional IVF. For these couples, ICSI offers the last possibility of conceiving a child with assisted reproduction.

Microinjection of the spermatozoa directly into the oocyte's cytoplasm can bypass all potential oocyte barriers as well as
activate its development (Uehara and Yanagimachi, 1976). The success of this technique in experimental animals led to the clinical application of ICSI to human gametes (Lanzendorf et al., 1988). The report of the first human pregnancies and births after ICSI encouraged the clinical use of this procedure in women who had failed to achieve fertilization in classic IVF or in those couples with extreme oligoasthenoteratozoospermia in the male partner (Palermo et al., 1992). At least in the short term, the offspring do not show an increase in congenital abnormalities (Bonduelle et al., 1994). Considering the first ICSI series of 161 treatment cycles at the Centre for Reproductive Medicine at Lübeck Medical School, Lübeck, Germany, we achieved a fertilization rate of 64% and a clinical pregnancy rate of 28%. ICSI seems to be the only successful method of assisted reproduction in cases of severe male subfertility, where low sperm count, extremely low motility and poor morphology do not allow fertilization by classic IVF. Using ICSI, the sperm quality does not seem to be important and fertilization and pregnancy rates are independent of sperm quality.

One last issue must be addressed briefly: except for completely paralyzed men, all of our patients require anesthesia for the RPE procedure. This particular patient had repeated transrectal stimulations under general anesthesia and no complications occurred. Although this very low complication rate is the rule, we try to keep the number of necessary stimulations to as few as possible. In the past, it was our policy to perform two RPE to establish the baseline sperm quality of the individual patient, and four to six cycles of timed electroejaculation in combination with IUI before turning to IVF for those couples failing to achieve conception (Ohl et al., 1991). With the possibility of ICSI for extremely poor sperm quality, we are rapidly changing our policy so that only one so-called test stimulation is performed and ICSI is proposed earlier to those couples not conceiving a pregnancy after a reasonable number of IUI cycles. It is too early to establish the ideal number of cycles, but this case report illustrates how the close cooperation between different reproductive disciplines not only leads to success for an individual couple but is also beneficial for future patients.

In conclusion, the combination of RPE and ICSI can make parenthood possible for couples in whom the husband suffers from a neurogenic loss of seminal emission and whose sperm quality is so low that conventional methods of IVF are not possible. The use of ICSI will also allow us to reduce the number of necessary RPE and consequently (for most men) the number of general anesthesia procedures.

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References


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