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Case Report

The delivery of the first babies conceived using testicular sperm in Northern Ireland

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This paper reports the delivery of infants conceived using testicular sperm aspirated from men with previously untreatable obstructive azoospermia.

CASE REPORT 1 Mr and Mrs C were aged 35. Mr C worked as a bus driver and his wife as a manageress. He was known to have obstructive azoospermia due to congenital absence of the vas deferens and was a carrier of the cystic fibrosis gene mutation R560T. His karyotype was 46XY and his hormone profile was normal. Mrs C was not a cystic fibrosis carrier, her menstrual cycle was regular and she was ovulating normally. She underwent ovulation induction for oocyte retrieval with subcutaneous injections of recombinant FSH (Puregon®, Organon) using a standard protocol. Transvaginal ultrasound guided oocyte retrieval was performed in August 1998 under intravenous sedation. Following retrieval, oocytes were incubated for 2 hours and then denuded of their cumulus matrix and coronal cells using hyaluronidase (80 IU/ml, IVF Science, Scandinavia) permitting assessment of oocyte maturity.

On the same day Mr C underwent testicular biopsy. Briefly, 10 ml of 0.5% bupivacine were injected around the spermatic cord. Two biopsies were taken using a 14 gauge Trucut needle (Baxter Healthcare Ltd, Norfolk, U.K.) inserted into the lower pole of the testis and advanced one centimetre. Sperm were retrieved from the biopsy sample by milking the seminiferous tubules with size 5 jeweller's forceps and enumerated after washing with in vitro fertilisation (IVF) media (Medicult, U.K.). Sperm were incubated for 3-4 hours at 37°C in 5% carbon dioxide prior to injection.

Only metaphase II oocytes with one polar body extruded were considered suitable for injection. Testicular spermatozoa were identified, retrieved from an IVF media drop and then placed in polyvinylpyrrolidine (PVP, Hunter Scientific, U.K.) using an Olympus JX50 micromanipulation microscope (Research Instruments, Cornwall, U.K.). After immobilisation of the twitching spermatozoa, metaphase II oocytes were injected and subsequently assessed for presence of pronuclei 16-18 hours later. Normally fertilised oocytes with two pronuclei were then incubated for 48-72 hours and the two embryos of highest quality transferred.

Mrs C had 21 oocytes retrieved and of these 19 were suitable for injection. Subsequently 10 of the injected oocytes fertilised normally and 2 embryos were replaced. Of the remaining embryos, 6 were suitable for storage. In September 1998 pregnancy test was positive and on transvaginal scan a viable twin pregnancy was confirmed.

In March 1999 healthy twin boys were delivered by emergency caesarean section at 31 weeks because of preterm labour. They weighed 1.7 and 1.5 kg and were phenotypically normal.

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CASE REPORT 2 Mr M was aged 29 and worked as a sales manager and his wife was aged 27 and was a nurse. Mr M had unexplained obstructive azoospermia with normal karyotype and hormone profile. Mrs M had a regular cycle and was ovulating normally.

In June 1998 Mr M had a testicular biopsy carried out under local anaesthetic as described in Case 1. Once the sperm had been milked from the seminiferous tubules they were stored in liquid nitrogen in multiple aliquots. Assessment of one stored aliquot to confirm sperm motility and hence viability post-thaw indicated suitability for future use. Freeze- thawed sperm were also incubated for 3-4 hours at 37°C in 5% carbon dioxide prior to injection.

Mrs M proceeded to ovulation induction and oocyte retrieval in July 1998. On the same day the sperm sample was thawed and the oocytes injected with freeze-thawed testicular sperm. Eight oocytes were collected, six injected with thawed testicular sperm and three fertilised nonnally. Two embryos were replaced and the remaining embryo was not suitable for storage. Transvaginal scan in September 1998 confirmed a singleton viable fetus. In April 1999 a healthy male infant weighing 3.7 kg was delivered at 38 weeks gestation by elective caesarean section.

DISCUSSION

In this paper we have reported the first ICSI babies to be conceived and delivered in Northern Ireland using fresh and freeze-thawed testicular sperm.

Azoospermia is the complete lack of sperm in the ejaculate and it occurs in about 2% of infertile men. Two thirds are due to genital tract obstruction and one third to germinal epithelium failure. In obstructive azoospermia spermatogenesis is known to be normal.[1] Men with obstructive azoospermia were considered to be untreatable until the advent of intracytoplasmic sperm injection (ICSI) in 1992.[2] With this technique one sperm is injected directly into the cytoplasm of the oocyte and excellent success rates have been reported for men with very poor semen quality.[3] In obstructive azoospermia, because spermatogenesis is normal, small numbers of sperm can be obtained from the testis or epididymis by open or needle biopsies.[4,5] However, as these sperm tend to be immotile they are unsuitable for standard in vitro fertilisation (IVF) but can be used for ICSI because motiliy is not required.[6] Since the first ICSI pregnancy using testicular sperm was reported in 1993 this procedure has become a standard treatment for men with obstructive azoospermia.[7]

Sperm have even been obtained from the testes of non-obstructive azoospermics and pregnancies have been reported using sperm from men with Klinefelter's syndrome (47XXY) for ICSI. However, the offspring of pregnancies conceived using sperm from men with non-obstructive azoospermia need to be carefully monitored in the future because spermatogenesis is grossly defective in these subjects, carrying a risk of genetic abnormality especially when the quality of the genome is unknown.[8]

All three of Northern Ireland's first testicular sperm ICSI children were phenotypically normal boys. Whether or not they are infertile like their fathers will not however, become obvious for many years to come.

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