CASE REPORT

Triplet pregnancy and delivery after intracytoplasmic injection of round-headed spermatozoa

Z.M.Kilani1,3, M.A.Shaban2, S.D.Ghunaim1, S.S.Keilani1 and A.I. Dakkak1

1The Farah Hospital, Zahran, PO Box 5323, Amman 11183 and
2Faculty of Medicine, University of Jordan, Amman 11942, Jordan
3To whom correspondence should be addressed

Intracytoplasmic sperm injection (ICSI) of round-headed spermatozoa into mature oocyte resulted in normal fertilization, embryo development and pregnancy in a 28 year old female. The husband had a long history of primary infertility. Three ICSI attempts were carried out and fertilization and embryo development occurred in all trials. However, only the third trial led to a pregnancy, which proved to be quadruplet after the transfer of four embryos. One embryo vanished and the remaining triplets were delivered at 35 weeks of gestation by Caesarean section. Two of the babies, a boy weighing 2000 g and a girl weighing 2250 g at birth were discharged in a good condition 1 week after delivery and the third baby, a boy weighing 1550 g, was discharged 3 weeks after delivery.

Key words: globozoospermia/ICSI/infertility/triplet delivery/triplet pregnancy

Introduction

Globozoospermia or the occurrence of round-headed spermatozoa, with different morphological and functional abnormalities, has been described (Schirren-Holstein, 1971; Lalonde, 1988; Escalier, 1990; Singh, 1992). The major abnormalities in such spermatozoa are to be found in the acrosome. Such abnormalities involve absence of certain acrosomal structures and/or proteinase activity (Schill, 1991; Singh, 1992) and anomalous distribution of nuclear basic proteins (Blanchard et al., 1990). Lack of acrosomal enzymes leading to absence of spermatozoa binding to the zona pellucida receptors has been described by Weissenberg et al. (1983) and Von Bernhardi et al. (1990). Although round-headed spermatozoa fail to bind to zona pellucida free hamster oocytes (Sym et al., 1984; Aitken et al., 1990), nuclear decondensation has been achieved when nuclei of round-headed spermatozoa were incubated with the cytoplasm of hamster oocytes (Sym et al., 1984). The presence of such abnormalities in the spermatozoon head does not necessarily mean a higher rate of chromosomal abnormalities, as demonstrated when round-headed spermatozoa were injected into mouse oocytes (Rybouchkin, 1996). Also such spermatozoa maintain normal motility, as determined by functional tests (Check et al., 1993).

Globozoospermic males used to be considered as sterile since their spermatozoa are unable to bind to the zona pellucida and penetrate the oocyte during standard in-vitro fertilization (IVF) (Schmiady et al., 1992) or to penetrate the nucleus after subzonal sperm injection (Dale et al., 1994). However, the development of intracytoplasmic sperm injection (ICSI) technology has opened up new possibilities for couples with male infertility due to globozoospermia and this has led to fertilization and embryo development (Bourne et al., 1995), pregnancy (Lundin et al., 1994; Liu et al., 1995), and birth of a healthy baby (Trokoudes et al., 1995). Here we report a triplet pregnancy and delivery (at 35 weeks’ gestation) after ICSI with round-headed spermatozoa.

Case report

The present couple suffered from primary infertility of 2 years’ duration. The husband, 52 years of age, had a previous childless marriage of 10 years. On physical examination, his genitals and hormonal profile were normal. Semen analysis showed significant presence of 100% round-headed spermatozoa on more than one occasion, otherwise the spermogram was normal. The wife was 28 years old. Gynaecological examination and hormonal profiles proved to be normal. Assisted fertilization was advocated. A first ovarian stimulation cycle was carried out using the short protocol with 0.1 mg Decapeptyl® (Ipsen Biotec., Paris, France) daily s.c. injection but no pregnancy occurred. In 34 h of HCG injection, seven oocytes in metaphase II were retrieved transvaginally under ultrasound guidance. ICSI as described by Palermo et al. (1992) and Van Steirteghem (1993) was performed. Three oocytes were fertilized and resulted in one embryo of grade I and two others of grade II according to Dokras et al. (1993). An easy embryo transfer was carried out using a Wallace catheter but no pregnancy occurred. In the second ICSI attempt, the short protocol was repeated for ovarian stimulation. Decapeptyl® 0.1 mg s.c. injection was used on day 2 of the cycle followed by daily injections of HCG; Profasi® (Serono, Rome Italy) were injected i.m. After 34 h of HCG injection, seven oocytes in metaphase II were retrieved transvaginally under ultrasound guidance. ICSI as described by Palermo et al. (1992) and Van Steirteghem (1993) was performed. Three oocytes were fertilized and resulted in one embryo of grade I and two others of grade II according to Dokras et al. (1993). An easy embryo transfer was carried out using a Wallace catheter but no pregnancy occurred. In the second ICSI attempt, the short protocol was repeated for ovarian stimulation. Decapeptyl® 0.1 mg s.c. injection was used on day 2 of the cycle followed by daily injections of
supported by 40 mg oral progesterone (Duphaston®; Solvay). Headed spermatozoon, leading to eight embryos. Four embryos and the follicular growth. Nine oocytes in metaphase II were adjusted according to the serum concentration of oestradiol.

2×75 IU follicle-stimulating hormone (FSH) (Metrodin®; Serono, Rome, Italy) from the 3rd day of the cycle and lasting for 8 days. Four oocyte complexes scored as MII were retrieved 34 h after HCG injection. Two out of the four oocytes were fertilized and cleaved. Two embryos of grade II were transferred but no pregnancy was obtained.

In the third ICSI attempt, the long protocol was applied using Zoladex® (Zeneca Ltd, Macclesfield, Cheshire, UK) with a 3.6 mg s.c. injection on day 21 of the foregoing cycle, for pituitary desensitization. Once pituitary desensitization was achieved (15 days after Zoladex®), three ampoules of Metrodin® were injected over 3 days and then the dose of Metrodin® was adjusted according to the serum concentration of oestradiol and the follicular growth. Nine oocytes in metaphase II were retrieved transvaginally 35 h after 10 000 IU of HCG injection. Each of the nine oocytes was micro-inseminated with a round-headed spermatozoon, leading to eight embryos. Four embryos grade I were transferred easily and the luteal phase was supported by 40 mg oral progesterone (Duphaston®; Solvay Duphar B.V., Weesp, The Netherlands) daily. The remaining four embryos were frozen. Pregnancy was established by positive HCG in the plasma (2 weeks after transfer) and later confirmed by ultrasound. Four sacs could be demonstrated in the uterine cavity by ultrasonography. However, subsequent follow-up showed one vanishing embryo and three surviving ones. The pregnancy was strictly monitored. A special protocol for high order pregnancy was followed. It included daily progesterone and Ascriptin® (Rorer Doma, Amman, Jordan) treatment in addition to salbutamol from the 20th week of pregnancy and dexamethasone from the 22nd week of pregnancy. After an uneventful pregnancy, three healthy babies were delivered by elective Caesarean section at 35 weeks of gestation: two boys weighing 2000 and 1550 g and one girl weighing 2250 g. The heavier boy and the girl were discharged 3 weeks after delivery. Six months later they were in good health, with a normal rate of growth and development.

A summary of the results is shown in Table I.

<table>
<thead>
<tr>
<th>Cycle number</th>
<th>Number of MII oocytes</th>
<th>2 PN Grade I embryos</th>
<th>Grade II embryos</th>
<th>Transferred embryos</th>
<th>Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>7</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>II</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>III</td>
<td>9</td>
<td>8</td>
<td>6</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

PN = pronuclei.

Since the introduction of ICSI, it has been useful to offer this technique to males who are infertile due to the round-headed spermatozoa. ICSI has led to fertilization, embryo development and pregnancy (Lundin et al., 1994; Bourne et al., 1995; Liu et al., 1995) and delivery of the first baby (Trokoudes et al., 1995). A fertilization rate of 50% was reported by Trokoudes et al. (1995) and a much lower one by Liu (1995). The fertilization rate reported here in the three cycles is 65% which may be attributed to the vigorous stimulation of the oocyte by the injecting needle during ICSI procedure. The recent finding by Rybouchkin et al. (1996) that round-headed spermatozoa are able to activate mouse oocyte only after parthogenic activation may suggest that oocyte activation after ICSI using round-headed spermatozoa is mandatory. More studies using oocyte activation are needed. Although Rybouchkin et al. (1996) demonstrated the presence of normal karyotypes in round-headed spermatozoa, the detailed nuclear criteria remains to be studied. It is hoped in the future that the semen of the offspring of these patients will be studied to obtain more data. To the best of our knowledge, this report is of the only triplet pregnancy and delivery obtained with a globozoospermic ICSI cycle. The findings in this case and the previously reported cases emphasize the fact that such morphological abnormalities are no longer considered reasons for infertility. Thus recently reported normal karyotypes (Rybouchkin et al., 1996) in round-headed spermatozoa and better understanding of the underlying pathology as well as the progress in ICSI technology and the successful pregnancies and deliveries of normal babies strengthen the belief that patients with globozoospermia can have their own children. In conclusion, this case emphasizes the fact that once the zona pellucida and the oolemma are bypassed, round-headed spermatozoa can fertilize the oocyte, leading to embryo development and pregnancy.

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References

ICSI using round-headed spermatozoa


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