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Case Study

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INTRACYTOPLASMIC SPERM INJECTION IN PARTIAL GLOBOZOOSPERMIA-A CASE STUDY

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ABSTRACT

Partial globozoospermia (PG) is a currently described kind of tera-tozoospermia that is characterized by an elevated amount of round-headed sperm cells and traditional acrosome defects. Remarkably, the oval spermatozoa derived from PG patients show an elevated incidence of differentiation defects as well. To compare the result of intracytoplasmic sperm injection (ICSI) in patient couples the place the male accomplice has partial globozoospermia with the effect in an accepted ICSI population. In the partial globozoospermia group, the stay birth charge used to be 66.7% in contrast with 50.0% in the control group. In partial globozoospermia, three out of 21 pregnancies ended in a miscarriage, one important beginning defect occurred, and one pregnancy ended in a neonatal loss of life due to sepsis in a premature child, in contrast with 4 stillborn in the control group. ICSI is a high-quality treatment in couples that failed to conceive spontaneously within 1 year blended with male infertility due to partial globozoospermia. The fertilization fees and the live beginning fees in this unique group did no longer range from those of the established ICSI population.

KEYWORDS: Partial globozoospermia, sperm morphology disorder, ICSI.

I INTRODUCTION

Partial globozoospermia (PG) may be a recently described sort of tera-tozoospermia that's characterized by an increased amount of round-headed sperm cells and typical acrosome defects. Remarkably, the oval spermatozoa derived from PG patients display an increased incidence of differentiation defects also. Although the round-headed cells that are present in partial and total globozoospermia appear alike regarding additional structural defects, partial and complete globozoospermia may represent different disorders.[1] The primary pregnancy using round-headed spermatozoa derived from a patient affected by total globozoo-spermia was achieved in 1994 with the utilization of intracytoplasmic sperm injection (ICSI).[2] In subsequent cases, fertilization rates were poor in 50%.[3] The poor fertilization rates with ICSI could also be thanks to deficient oocyte activation by these spermatozoa.[4] Oocyte activation with calcium ionophores or elec-tric activation has been applied in some studies and resulted in better fertilization rates in most cases.[3,5-11] To our knowledge, no augmented risk on congenital abnormalities has been reported in such pregnancies. In partial globozoospermia, the ejaculate contains not only round-headed spermatozoa, but also a certain percentage of normal sperm cells.[1] A spontaneous conception is therefore possible in theory, although we expect that these patients may have impaired fertility and a requirement for medical assistance in conceiving a toddler. To date, there are not any studies on the necessity and therefore the efficacy of assisted reproductive techniques (ART) during this specific group of patients. Because we found defects in spermatozoa that appeared normally shaped in an earlier study[1], this disorder may cause an unknown cause for poor fertilization, as in total globozoospermia. The aim of this study was therefore to assess the success rate also because the possible adverse risks of ART for patients affected by this rare quite teratozoospermia.

Partial Globozoospermia Group

Research place: International Fertility Canter, New Delhi, India. In total, 42 couples were identified with the male partner presenting with partial globozoospermia (>25% round-headed or acrosomeless sperm cells in the ejaculate). All of the couples suffered from a primary fertility disorder. These couples were enrolled in our assisted fertility program. Ten couples eventually did not receive any treatment. Three of these couples (patients 3, 5, and 6) conceived spontaneously with a time to pregnancy between 1 and 3 years. Two patients (patients 1 and 8) decided not to make use of assisted reproductive technologies (ART), and finally, five couples were referred elsewhere for treatment (patients 2, 4, 7, 9,

and 10). The remaining 32 couples received ART IUI, IVF, or ICSI at our center. A flow chart of the patient treatment and out-comes is shown in. Two out of the three couples undergoing IUI (patients 11 and 12) conceived after six and four cycles, respectively. The third couple ceased treatment after two cycles (patient 13). IVF was performed in eight couples: Total fertilization failure occurred in five couples (patients 15, 17–19, and 21), and poor fertilization (27% and 8%, respectively) in two cou-ples (patients 16 and 20). These seven couples were referred for ICSI. The last couple ceased treatment after two cycles of IVF (patient 14). From the 28 couples that started ICSI treat-ment (patients 22–42), one couple was excluded for further analysis because no ovum pick-up (OPU) could be performed (patient 22). We compared the outcome of the 27 PG patient couples who underwent ICSI with the outcome in a general ICSI pop-ulation with no known partial globozoospermia.

Control Subjects

Each PG patient couple that was treated with ICSI was intended to be matched with ten control couples. For seven control couples, sufficient data weren't available, and that they were therefore excluded from further analysis, leading to a complete of 263 control couples and 27 PG couples for comparative analysis. Matching was performed during a random fashion from the cohort of couples receiving ICSI in our center. Matching criteria were female age at the time of the primary OPU and year of the primary ICSI cycle. These matching criteria were chosen for the documented influence of female age on ART outcome and to catch up on slight changes in protocols which will have occurred over the years, respectively. All control couples suffered from a primary fertility disorder, they were selected for treatment consistent with the rule, and none of the male partners suffered from (partial) globozoospermia.

ICSI Treatment

Only the first ICSI treatment was included for analysis. Note that a single treatment may contain several ICSI cycles (1–10 cycles in this study). Ovarian stimulation was performed by administration of GnRH agonist starting on day 21 of the previous cycle, followed by a stimulation phase with recombinant FSH. OPU was planned when R13 follicles with a diameter of >18 mm were observed by ultrasound examination, and OPU was performed 36 hours after hCG injection. ICSI was performed basically as described previously by Palermo et al.[12] Fertilization rates were scored 18–22 hours after the ICSI procedure. On day 3 after OPU, the embryos were scored regarding number of blastomeres and percentage of fragmentation. Embryos were classified as A, B or C, with A embryos having the highest chance of implantation and C embryos the lowest. The best embryos were selected for single-embryo transfer (SET) or double-embryo transfer (DET). Embryo cryopres-ervation was performed on surplus class A embryos. A pregnancy test was performed on day 18 after OPU, and an ultrasound was made 3–5 weeks after the embryo transfer. One or more intrauterine gestational sacs and fetal heartbeat were considered to indicate a pregnancy. A miscarriage was considered as such before 16 weeks of gestation. Pregnancy and neonatal outcome were collected by patient questionnaires.[13]

II CASE REPORT

This study was 42 sub fertile couples in which the male suffered from partial globozoospermia were identified. Of these 42 couples, 27 underwent ICSI. Research place: International Fertility Canter, New Delhi, India from July- December 2019. The first ICSI treatments of PG patient couples were included for analysis and were matched with 263 first ICSI treatments in the control group. The patient semen parameters with the fertility treatment and outcome. In the patient couples that conceived spontaneously or by IUI, no more than a mild oligozoospermia or asthenozoospermia was found in the semen analysis, rather than an obvious teratozoospermia. Although these values are not that different from the semen analysis of the couples that initially underwent IVF and were found to have a poor fertilization rate, they are different from the values of the patients that underwent ICSI as initial treatment (concentration: P<.001; motility: P¼.012). The mean semen parameters, including the percentage of acro-someless sperm cells, were not significantly different between the pregnant and no pregnant ICSI couples. The patient and control groups were similar regarding female age because this was a matching criterion. Also, duration of the fertility disorder, duration of the treatment, and number of ICSI cycles were similar in the two groups. No significant differences were found for number of oocytes obtained per cycle, fertilization rate, percentage of transferred A, B, or C embryos, or ability to freeze spare embryos. Primary and secondary outcomes measures are presented. The live birth rate in the patient group was higher compared with the control group (66.7% versus 50.0%, respectively), but this difference did not reach statistical significance (Fisher exact test: P¼.09). The secondary outcome measures were not significantly different, either: pregnancy rate 74.1% versus 57.6% (Fisher exact test: P¼.10); miscar-riage 14.3% versus 18.5% (Fisher exact test: P¼.77); and twin pregnancy 14.3% versus 21.6% (Fisher exact test: P¼.58). No stillborns occurred in the patient group, compared with one stillborn in a singleton pregnancy and three still-borns as part of a twin pregnancy in the control group. Information on the sex, gestational age, birth weight, and congenital abnormalities of the newborns in the PG group were obtained for 17 out of 18 cases. In this group, 6 boys and 11 girls were born. Mean gestational age was 38 weeks 1 day. Mean birth weight was 2,993.6 grams (within 20th– 50th percentiles). One case of mild aortic coarctation was re-ported. One child died in the neonatal period (day 10) because of sepsis in prematurity (28 weeks 1day).

III DISCUSSION

In this study, we report on the efficacy and safety of ICSI as a treatment for infertility due to partial globozoospermia, of which disorder little is known to date. We show that this group of couples performed at least equally to a general ICSI population regarding the live birth rate. This is a reassuring finding for patients with partial globozoospermia. We chose to describe all 42 PG patients that were identified in an 8-year period at our center, and subsequently we chose to perform a pertreatment analysis (possibly including several ICSI cycles) rather than an analysis per ICSI cycle. We did so because we think that the combination of description and case-control analysis provides us with the ingredients for proper counseling of patients suffering from partial globo-zoospermia about their chances of conceiving a child at the start of an ART treatment. From these data, we can conclude that spontaneous pregnancies can occur in cases with normal to mild oligospermia in combination with a mild asthenozoospermia and teratozoospermia (according to World Health Organization criteria.[14] Whenever spermatozoa with acrosomes are present, spontaneous conception can occur but possibly with a longer time to pregnancy, as was observed in three patient couples. This suggests that PG may occur more often than expected in a proven fertile population. When, however, patients do not conceive spontaneously within a reasonable period of 1 year, or even via IUI when the semen parameters are acceptable to do so, ICSI seems to be the optimal treatment, because poor fertilization or even total fertilization failure appears to be a common result after IVF. We could not find a significant difference in any of the investigated parameters (including fertilization rate, percentage of quality A embryos, percentage of cryopreserved embryos of good quality, pregnancy rate, percentage of mis-carriages, and live birth rate) between the PG and control groups. In fact, these couples performed somewhat better on the last three items, though not significantly. In addition, the follow-up of 17 out of the 18 children born in the patient group was also reassuring. No aberrations regarding gesta-tional age at time of birth or birth weight (which was within the 20th–50th percentile) were found. In one child out of the 18, a congenital disorder was observed, namely, an aortic coarctation, representing a prevalence of 5.6%. Compared with the odds ratio for birth defects after ICSI (between from 1.4% to 2.0%[15], this is a high figure. We should, however, take the small sample size of our group into consideration before drawing any conclusions. Obviously, future research should focus on the occurrence of birth defects in a larger group of partial globozoospermia patients. The data should then be linked to studies on the molecular aspects of partial globozoospermia regarding DNA damage and/or possible genomic anomalies in the sperm head. In one case a neonatal death was observed. This death occurred because of sepsis in a premature infant on the tenth day after birth. It is not probable that this neonatal death was causally linked to ICSI in general or ICSI with semen derived from partial globozoospermia patient in particular. The round-headed spermatozoa in partial globozoospermia share a lot of characteristics with those found in total globozoospermia.[1] In total globozoospermia, a reduced ability to fertilize is described in about one-half of the cases reported, for which oocyte activation is applied in various reports.[5-11,16] Because a previous study from our group[1], demonstrated an increased occurrence of structural abnormalities in ‘‘normal’’ oval spermatozoa derived from PG men, we anticipated that these ‘‘normal cells’’ that are picked for ICSI could have the impaired ability to fertilize in common with total globozoospermia. Interestingly, fertilization via ICSI does not appear to be negatively affected by these abnormalities, but they may still play a role in spontaneous fertilization or fertilization via IVF, so further research on partial globozoo-spermia is still warranted regarding this aspect. In reviewing our data, we can conclude that we are now better equipped to counsel subfertile couples with partial globozoospermia. In daily practice, ICSI is offered when total fertilization failure occurs in IVF. Patients are counseled and treated according to this guideline.[17] First, their chance to conceive spontane-ously is lower compared with the normal population, but this chance is by no means absent, provided that the other semen parameters are favorable. When enrolled in a fertility program, however, ICSI is the treatment of choice. Second, their chance of conceiving a child via ICSI seems to be at least similar to the general ICSI population. Finally, there appears to be no increased risk for a miscarriage. Unfortunately, we cannot yet counsel on the risk of congenital anomalies in this population, because our study group is too small to draw definite conclusions on this aspect of the treatment.

IV CONCLUSION

ICSI is an effective treatment in couples that failed to conceive spontaneously within 1 year combined with male infertility due to partial globozoospermia. The fertilization rates and the live birth rates in this specific group did not differ from those of the general ICSI population. This study shows that that in compromised male fertility due to partial globozoospermia, ICSI is an adequate treatment to get pregnant, although spontaneous pregnancies cannot be excluded. Pending future research on the ICSI results in a larger study, including the prevalence of birth defects and the molecular aspects of the sperm heads in this population, these patients should be reassured that they have a good chance to father a healthy child.

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