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Gestational surrogacy: a feasible option for patients with Rokitansky syndrome

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Rokitansky syndrome is a developmental defect characterized by agenesis of the uterus and vagina but normal gonads and secondary sexual characters. It is not commonly transmitted as a dominant genetic trait. Surrogacy, which is legally and ethically accepted in the UK and other countries, has made it possible for the patients with this syndrome to have their own genetic children. Six patients with Rokitansky syndrome underwent 11 ovarian stimulation cycles that resulted in 11 fresh and three frozen embryo transfer procedures into six prospective surrogate mothers. Both commissioning and surrogate couples were properly screened and counselled and their treatment was approved by the clinic internal review committee (ethics committee). The treatment cycles resulted in six clinical pregnancies (42.9% pregnancy rate per embryo transfer and 54.5% per oocyte retrieval) and three live births (21.4% per embryo transfer, 27.3% per retrieval and 50% per patient). Gestational surrogacy is a viable treatment for patients with Rokitansky syndrome. Such patients should be well informed and supported to be able to have a family using their own genetic gametes.

Key words: congenital absence of uterus/IVF/Rokitansky syndrome/surrogacy

Introduction

Mayer-Rokitansky-Kuster-Hauser syndrome is a complex developmental defect characterized by complete or partial agenesis of the vagina and uterus associated with normal external genitalia and gonads. Complete vaginal aplasia may be accompanied by rudimentary cornua caused by premature termination of recannulation of the Müllerian ducts.

The syndrome was first described by Rokitansky in 1838. Mayer, Kuster and Hauser later contributed to the description as a spectrum of Müllerian anomalies, including vaginal agenesis with or without renal anomalies in genotypic and phenotypic female subjects with normal endocrine status (Ghirardini and Popp, 1995). There has not been any cause identified for this condition and the incidence is 1 in 4500 new-born babies (Egarter and Huber, 1988).

Until recently, the main interest in these cases revolved around reconstructive surgery, either laparoscopically or via laparotomy; the different methods of creation of an artificial vagina were the centre of discussion (Chapron *et al*., 1995; Cooper *et al*., 1996; Fedele *et al*., 1996).

New techniques of assisted conception have the potential to enable these patients to fulfil their reproductive aspirations. Recently a large retrospective study in the USA showed that congenital absence of the uterus and vagina is not commonly transmitted as a dominant genetic trait (Petroza *et al*., 1997)

Materials and methods

All gestational surrogacy cycles that took place in a private clinic in London, UK from January 1993 to November l996 were reviewed. Six patients with Rokitansky syndrome had 11 ovarian stimulation cycles that resulted in 11 fresh embryo transfer and three frozen embryo replacement procedures into six prospective surrogate mothers. The case notes were retrieved and reviewed in detail.

All patients attended the clinic with their partners for an initial consultation and subsequently recruited their own surrogate mother, either personally or through a charity agency. The prospective commissioning (genetic) and surrogate parents were clinically assessed and screened for infectious diseases. To avoid the risk of human immunodeficiency virus (HIV) transmission, semen samples of the commissioning fathers were frozen and quarantined until they had a repeat negative HIV test 6 months later. As Rokitansky syndrome did not have a clear genetic pattern, commissioning parents preferred to use their own genetic rather than donated oocytes. However, they were counselled regarding the difficulty of making a definite statement about genetic risks. They were also counselled by two qualified independent counsellors, both individually and with their surrogate couple. Certain issues were agreed on by both prospective commissioning and surrogate couples, e.g. the number of embryos to be transferred, antenatal screening, chorionic villous sampling, amniocentesis, selective fetal reduction in case of multiple pregnancy, termination of pregnancy if necessary, etc. A good relationship between the commissioning and surrogate couples was established and the surrogacy arrangement was approved by the clinic's internal review committee (ethics committee). Members of the committee discussed ethical and social issues, particularly the welfare of the potential child and any existing children. Prospective commissioning and surrogate couples had legal advice and a contract was drawn up. The latter included the surrogate expenses and life insurance, and other legal issues related to the surrogacy arrangement and parenthood.

The mean age of the patients was 31.5 years (range 25–35) and they were all in their first attempt at assisted conception. All six patients completed at least one cycle of treatment (Table I). Prior vaginoplasty had been carried out in two patients and four others had

Table I. The outcome of 11 ovarian stimulation cycles for six patients with Rokitansky syndrome

Patient no.	Patient's age (years)	Oocyte retrieval cycles (*n*)	Total no. of oocytes (mean) (*n*)	Fertilized oocytes [(*n*) (%)]	Embryo transfer procedures (*n*)	No. of embryos/cycle	Frozen embryos (*n*)	Outcome
1	33	2	29 (14.5)	24 (82.7)	3 (2 fresh, 1 frozen)	2.6	18	Singleton (male)
2	25	1	18	18 (100)	1 (fresh)	2	15	Triplet (all male)
3	35	4	42 (10.5)	14 (33.3)	4 (fresh)	2.7	0	Miscarried twice
4	35	1	4	4 (100)	1 (fresh)	3	0	Twin (sex not known)
5	30	1	9	6 (66.7)	1 (fresh)	3	0	Miscarried
6	27	2	59 (29.5) 2 frozen)	45 (76.2)	4 (2 fresh,	2.7	34	Nil
Total (median)	33	11	161 (14.6)	111 (68.9)	14 (11 fresh	2.7	67 (6.1/cycle)	3 live births and 3 miscarriages

conservative management using vaginal dilators. The husbands' age range was 27–57 years and all had normal semen parameters and only in one case was intracytoplasmic sperm injection required due to poor post-thaw sperm parameters. The median age of the surrogate mothers was 34.5 years (range 29–39) and their median parity was 3 (range 2–4).

Prior to ovulation induction the commissioning mothers underwent serial hormonal and ultrasonic assessment to establish the pattern of each patient's normal ovarian cycle.

Ovulation was induced using the luteal phase protocol. Down-regulation was achieved by a single mid-luteal injection of Prostap 'SR' 3.75 mg (leuprolide acetate depot; Wyeth Laboratories, Maidenhead, UK) and confirmed by a vaginal ultrasound scan with or without oestradiol measurement at least 12 days later. Daily gonadotrophin injections were given for 12-16 days until the leading follicles were ~20 mm in diameter. Oocyte retrieval was performed 36 h following an injection of 10 000 IU of human chorionic gonadotrophin. All prospective commissioning mothers had vaginal oocyte retrieval except one who required laparoscopic oocyte retrieval as her ovaries were not accessible through the vagina. A natural cycle was used in one surrogate as she had previously experienced side-effects with a gonadotrophin-releasing hormone analogue. She abstained from sexual intercourse during the treatment cycle. All the other surrogates underwent down-regulation with leuprolide acetate injection 3.75 mg. When the commissioning mother started her gonadotrophin injections the surrogate mother started oral oestradiol valerate 2 mg twice daily. Luteal phase support was achieved with twice daily progesterone pessaries 400 mg (Cyclogest; Cox Pharmaceutical, Barnstaple, UK) that were in addition to the oestradiol valerate (Progynova tablets; Scherring Health Care, Burgess Hill, UK) 2 days prior to embryo transfer; the treatment continued until 12 weeks gestation. All treatment cycles were completed with successful embryo transfer.

Results

The six patients completed 11 oocyte retrieval procedures (average of 1.8 per patient). A total of 161 eggs was retrieved. The mean number of eggs collected per cycle was 14.6 (range 2-49). The fertilization rate was 68.9%. Either two or three embryos were transferred into the surrogate in each treatment cycle (average 2.7). A total of 67 embryos was cryopreserved (average of 6.1 embryos per cycle). A total of 11 fresh and three frozen embryo transfer procedures took place (18 embryos were thawed for the three frozen embryo replacement cycles) and there were still 49 frozen in storage. Five surrogates became pregnant at least once. The pregnancy rate was 42.9% per embryo transfer and 54.5% per ovarian stimulation cycle. Six babies [a singleton, (male) one set of twins (no record of their gender) and one set of triplets (all male)] have been delivered. The take-home baby rate was 21.4% per embryo transfer, 27.3% per ovarian stimulation cycle and 50% per patient, i.e. three of six patients were successful.

Discussion

Gestational surrogacy is a viable treatment for patients with Rokitansky syndrome. A medical literature search gave us access to a few articles about Mayer-Rokitansky-Kuster-Hauser syndrome, particularly about its classification (Tarry *et al*., 1986; Strubble *et al*., 1993; Fedele *et al*., 1996). Many of these papers have centred on the creation of a functional vagina, diagnosis and management of the sporadic cases (Muram and Jones, 1994; Russ *et al*., 1997; Giatras *et al*., 1998) and the recent advances in laparoscopic treatment compared to laparotomy (Popp and Ghirardini, 1992; Giraldo *et al*., 1996; Major *et al*., 1997). Only a handful of the papers reviewed the reproductive potential of these patients (Egarter and Huber, 1988; Yovich and Hoffman, 1988; Batzer *et al*., 1992).

It was stated in 1992 (Batzer *et al*., 1992) that the reported world experience with genetic offspring of patients with vaginal agenesis consisted of five pregnancies. Two pregnancies were from that report and three from two previous reports (Yovich and Hoffman, 1988; Utian *et al*., 1989). A large retrospective study was presented in 1997 (Petroza *et al*., 1997) with many more treatment cycles for patients with Rokitansky syndrome attempted to determine if there was an inheritance pattern of the syndrome through a questionnaire distributed to all the centres performing surrogacy treatment in the USA. A total of 162 IVF/surrogacy treatment cycles performed for 58 patients with congenital agenesis of the uterus and vagina was reviewed. The treatment resulted in 34 live births (17 female and 17 male). One male child was diagnosed with an non-specific middle ear defect and hearing loss. They concluded that congenital absence of the uterus and vagina was not inherited commonly in a dominant fashion. Another group

(Serafini *et al*., 1994) reviewed all surrogacy treatment cycles including those for patients with Rokitansky syndrome from four centres in the USA. A total of 449 embryo transfer procedures to IVF/surrogates resulted in 127 (28%) clinical pregnancies and 101 (22%) live births/ongoing pregnancies. The age of the prospective genetic mother (commissioning mother) was a crucial factor in success. Those who were <39 years of age had a clinical pregnancy rate of 41% per embryo transfer and a 33% viability whereas those who were >40 years of age had a viability rate of 12.1% per embryo transfer. They did not present the results of patients with Rokitansky syndrome separately. In an article entitled 'Gestational carrier pregnancy' (Corson *et al*., 1998) five carrier conceptions were reported for five out of 11 patients with Rokitansky syndrome. There was no detailed information about the number of treatment cycles or live births in this group. In 144 embryo transfer surrogacy cycles (120 fresh and 24 frozen embryo replacement) for 75 patients with various indications, 37 pregnancies were reported at a rate of 25.7% per embryo transfer and 49.3% per patient. A very poor outcome of surrogacy treatment was reported for nine patients (commissioning mothers) aged ⩾40 years; and no pregnancies in 26 fresh embryo transfer cycles and one frozen embryo replacement cycle. We have presented here the largest single series of its kind in the UK, which confirmed the fact that women with the Rokitansky syndrome have a good reproductive potential compared with their counterparts in the normal population. All our patients had been diagnosed and treated in their adolescent years and had knowledge of their inability to conceive.

In future, we speculate that these patients will seek advice much earlier as IVF technology will be more widespread and more accessible. Detailed information and counselling in young adulthood will play an important role. In this retrospective analysis we did not discuss legal issues concerning surrogacy and related matters in detail. We believe that patients with Rokitansky syndrome should be informed and supported, morally and financially, so they are able to have a family using their own genetic gametes before their reproductive age is over.

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