Management of Transient Ovarian Failure: Pregnancy After In Vitro Fertilization and Intracytoplasmic Sperm Injection—A Case Report

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Submitted: October 2, 1997

Accepted: October 10, 1997

Purpose: The case history of a 36-year-old patient with transient ovarian failure, presumably induced by previous ovarian surgery and a recent pelvic inflammatory disease, is described.

Methods: During several months, the patient underwent transvaginal ultrasound and hormonal follow-up. Ovulation was triggered by hCG in a cycle in which spontaneous follicular ripening had occurred. Transvaginal puncture of the single follicle was performed for in vitro fertilization.

Results: One oocyte was retrieved and fertilized by intracytoplasmic sperm injection, giving rise to a single good-quality embryo. A singleton pregnancy, which ended in the birth of a healthy daughter, was established.

Conclusions: This case demonstrates that it is worthwhile to monitor patients with transient ovarian failure closely, and if other infertility factors are present, IVF of one oocyte may be considered.

KEY WORDS: intracytoplasmic sperm injection; premature menopause; transient ovarian failure.

INTRODUCTION

Premature gonadal failure accounts for approximately 5% of all cases of infertility. Several methods for restoring ovarian function have been tried, but none of them has proved to have a predictable outcome. Spontaneous resumption of the ovarian function does occur, and ovulations and ensuing pregnancies have been reported (1). Treatment with estrogens becomes

mandatory when the hypoestrogenic condition persists for several months and there are indications that estrogens facilitate the resumption of ovarian function (2,3). When the infertility of a woman is due solely to premature ovarian failure, expectant observation, with or without estrogens, is the only advice that can be given to the patient. When infertility due to ovarian failure is compounded with another infertility factor, however, spontaneous conception is very unlikely. In this case, we decided that intermittent observation of follicular growth and oocyte retrieval for in vitro fertilization, when maturation of an oocyte occurred, provided a unique opportunity for treatment.

We report a pregnancy after intracytoplasmic sperm injection (ICSI) of a single oocyte retrieved during a spontaneous cycle in a woman with transient premature gonadal failure and impaired tubal patency.

CASE REPORT

A 36-year-old nulliparous woman was referred to the infertility clinic because of irregular cycles and infertility. Twelve months prior to referral a right oophorectomy and left ovarian cystectomy was performed because of bilateral benign ovarian cysts. During the first 8 months following this procedure, the menstrual cycle was interrupted and follicle stimulating hormone (FSH) levels were reported to be moderately elevated. However, at consultation the patient reported a regular menstrual cycle during the past months, indicating restored ovarian function. Baseline levels of gonadotropins were within the normal premenopausal range, and ovulation was confirmed by elevated progesterone levels in the luteal phase. Hysterosalpingography revealed patent tubes, and semen analysis was normal according to World Health Organization (WHO) criteria.

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The patient's medical and family history was unremarkable. Her menarche was at the age of 13, with regular 28-day cycles. She weighed 57 kg, was 169 cm in height, and had normal secondary sexual development. A pelvic examination was normal.

A few months later, while her infertility problem was being investigated, the patient was admitted to the hospital because of acute pelvic pain and fever. Laparoscopy revealed a pelvic inflammatory state with left purulent salpingitis and multiple tuboovarian adhesions. *Escherichia coli* was cultured from the peritoneal fluid. The patient was treated with cefazolin, 3 × 3 g a day (Cephacidal; Bristol-Myers SQUIBB), and metronidazole, 3 × 500 mg a day (Flagyl; Rhone-Poulenc Rorer) intravenously, and was discharged after 2 weeks when the inflammatory parameters had become normal. Following admission, she complained of hot flushes. Elevated gonadotropin levels suggested gonadal failure. Spontaneous conception was considered to be unlikely due to both gonadal failure and tubal incompetence. Therefore, it was proposed to monitor her FSH levels and to perform a trial of gonadotropin stimulation for in vitro fertilization (IVF). A phase of diminished FSH levels could signal resumption of normal ovarian function and sensibility to gonadotropin treatment. Initially, the monthly FSH levels revealed a slight decrease, but they remained hypergonadotropic thereafter for a longer period. Monitoring was stopped, and the patient was asked to return when menstruation occurred. A few months later, she came to see us 14 days after a spontaneous menstruation. Transvaginal sonography showed three follicles (mean diameters: 18, 17, and 20 mm), and the serum estradiol concentration was 181 pg/ml. Human chorionic gonadotropin (hCG; Pregnyl; Organon, Oss, The Netherlands), 5000 IU, was administered and oocyte retrieval was performed 36 hr later. A single oocyte was retrieved by transvaginal aspiration. Although the sperm count was normal according to WHO criteria, ICSI was preferred to exclude possible fertilization impairment. A good-quality embryo, according to a three-degree score, based on the size and equality of the blastomeres, as described by Puissant *et al.* (4), was obtained and transferred 48 hr later. The luteal phase was supported with hCG, 1500 IU, on days 5, 8, and 11. Fourteen days later determination of serum hCG indicated that implantation had occurred. Transvaginal ultrasound at 8 weeks of gestation showed a vital singleton pregnancy. At 38 weeks of gestation the patient delivered a healthy girl weighing 3090 g.

It is interesting to note that the patient was found to be in menopause 6 months after the birth of her child.

DISCUSSION

Premature gonadal failure is defined as hypergonadotropic amenorrhea occurring before the age of 40, and its incidence is estimated to be 1% (5). Several treatment modalities have been tried and pregnancies have been reported, both with and without treatment. However, spontaneous resumption of ovarian function or the outcome of treatment cannot be predicted. Since the advent of IVF, oocyte donation has been the most reliable method for obtaining a pregnancy, but this option was refused by our patient.

Ovarian surgery is associated with a shortening of the reproductive life span, due either to the altered vascularization of the ovary or to the sheer reduction of the number of available follicles. Although few data about the long-term effects of conservational ovarian surgery on future gonadal function are available, transient gonadal failure can be expected as a sequel of this intervention. Sayegh and Garcia (6) stated, in a retrospective review of 67 cases, that conservational ovarian surgery has no adverse effects on ovulatory function as assessed by menstrual patterns and conception rates over a prolonged period. On the other hand, it is well-known that in patients with previous ovarian surgery, the ovarian response to follicular stimulation is impeded as described by Hornstein *et al.* (7). It is also well-known that moderately elevated levels of FSH are associated with a poor ovarian response, and measurement of FSH at the beginning of the cycle is accepted as a reliable prognostic factor. When FSH levels are frankly elevated, however, stimulation with gonadotropins cannot be expected to elicit an ovarian response. Waiting for the occasional spontaneous resumption of ovarian function, and if some other infertility factor is also present, IVF in a natural cycle is the only option, provided the patient does not accept oocyte donation. The probability of pregnancy following IVF in a natural cycle is rather low and unknown in the group of women demonstrating transient ovarian failure. The outcome of treatment in our case illustrates that this policy is worth pursuing.

REFERENCES

1. Alper MM, Jolly EE, Garner PR: Pregnancies after premature ovarian failure. *Obstet Gynecol* 1986;67:59S-62S
2. Check JH, Chase S, Spence M: Pregnancy in premature ovarian failure after therapy with oral contraceptives despite resistance to previous human menopausal gonadotropin therapy. *Am J Obstet Gynecol* 1989;160:114-115

3. Tang L, Sawers RS: Twin pregnancy in premature ovarian failure after estrogen treatment: A case report. *Am J Obstet Gynecol* 1989;161:172-173
4. Puissant F, Van Rysselberge M, Barlow P, Deweze J, Leroy F: Embryo scoring as a prognostic tool in IVF treatment. *Hum Reprod* 1987;2:705-708
5. Coulam CB, Adamson SC, Annegers JR: Incidence of premature ovarian failure. *Obstet Gynecol* 1986;67:604
6. Sayegh R, Garcia CR: Ovarian function after conservational ovarian surgery: A long term follow-up study. *Int J Gynecol Obstet* 1992;39:303-309
7. Hornstein MD, Barbieri RL, McShane PM: Effects of previous ovarian surgery on the follicular response to ovulation induction in an in vitro fertilization program. *J Reprod Med* 1989;34: 277