ULTRASONOGRAPHY

Effect of a Sonographically Diffusely Enlarged Uterus Without Distinct Uterine Masses on the Outcome of In Vitro Fertilization–Embryo Transfer

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Purpose: Our objective was to study the effect of a sonographically diffusely enlarged uterus without distinct uterine masses on the outcome of in vitro fertilization–embryo transfer (IVF-ET).

Methods: Nineteen primary infertility patients undergoing IVF-ET who had a sonographically diffusely enlarged uterus without distinct uterine masses were enrolled. An age-controlled group of 144 primary infertility patients undergoing IVF-ET with a normal uterus and no history of uterine surgery was included.

Results: The age, day 3 follicle stimulating hormone, antral follicle count, ovarian response, endometrial thickness, number of retrieved and fertilized oocytes, number of transferred embryos, clinical pregnancy rate, and total delivery rate were not statistically different between the two groups ($P > 0.05$). Patients with a sonographically diffused enlarged uterus without distinct uterine masses had a higher spontaneous abortion rate (66.7%) than controls ($P < 0.04$; odds ratio = 7.5; 95% confidence interval, 1.16–48.56).

Conclusions: A high spontaneous abortion rate was found in patients with a sonographically diffusely enlarged uterus without distinct uterine masses undergoing IVF-ET. Enhanced luteal support was required.

KEY WORDS: IVF-ET; pregnancy outcome; spontaneous abortion; sonographically diffusely enlarged uterus.

INTRODUCTION

Infertile women with a sonographically diffusely enlarged uterus without distinct uterine masses are a particular group of patients. A clear-cut diagnosis is usually unavailable unless the patient undergoes conservative surgery due to chronic pelvic pain, massive vaginal bleeding, or infertility. Patients with a sonographically diffusely enlarged uterus without distinct uterine masses are highly related to adenomyosis (1), which is a common disease entity resulting in uterine enlargement, having detrimental effects on reproductive outcome (2), and causing obstetrical and gynecological complications (3,4). However, few data are available on the outcome of in vitro fertilization (IVF) in such patients. The aim of this study was to examine the effect of sonographically diffusely enlarged uterus without distinct uterine masses on the outcome of assisted reproduction.

MATERIALS AND METHODS

From January 1996 to December 1997, 19 patients who underwent IVF at our IVF unit who had a sonographical pattern of diffusely enlarged uterus without distinct uterine masses detected on day 3 were enrolled. An age-matched group of 144 women who had a normal uterus during this period were included as controls. Hysteroscopy was routinely performed on all patients to confirm a normal uterine cavity before IVF.

Ultrasound evaluation was carried out routinely for all patients on day 3 of the cycle between 0700 and

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0900 using an Accuson computed ultrasound 120XP/10 (Acuson Inc., Mountain View, CA) by one operator (C.-H.C.). A 7-MHz high-frequency transducer vaginal sector scanner and a 5-MHz transducer abdominal sector scanner were used. Both ovaries were scanned carefully and total antral follicles (2–8 mm) were counted (5,6). Patients with a sonographical pattern of diffusely enlarged uterus without distinct uterine masses were defined by the following criteria: the presence of a diffusely enlarged uterus and one or more heterogeneous myometrial areas not encapsulated and within round anechoic areas 1–3 mm in diameter (1). Any well-defined margins of heterogeneous structure and variable echogenicity were carefully excluded (7).

All patients received leuplide acetate (1 mg/day sc; Lupron; Abbot Australia Pty., Ltd., Kurnell, New South Wales, Australia) 10 days before the expected day of menstruation (long protocol) or on day 2 of menstruation (short protocol). This was continued through the treatment cycle until the time of human chorionic gonadotropin (hCG) administration. Two ampoules of follicle stimulating hormone (FSH; Metrodin; Serono Laboratories, Randolph, MA) and 2 ampoules of human menopausal gonadotropin (hMG; Pergonal; Serono Laboratories) were administered daily for the first 3 days. The dose was tailored according to the number and size of follicles as monitored daily using transvaginal ultrasound and serial serum estradiol levels. Ten thousand international units (IU) of hCG (Pregnyl; Organon, Oss, The Netherlands) was administered intramuscularly (i.m.) when the mean diameter of two or more leading follicles reached 16 mm. Transvaginal ovum retrieval was scheduled 36 hr later. Embryo transfer was performed 48–72 hr following fertilization. Luteal-phase support was supplied for all patients in the form of oral progesterone (Utrogestan; Laboratories Piette International, Brussels, Belgium) and hCG (Pregnyl) injections, 2500 IU i.m., every fourth day starting on the day of embryo transfer and continued for 2 weeks. A urine pregnancy test was performed 17 days after the transfer procedure. Clinical pregnancy was defined as the presence of at least one intrauterine gestational sac on transvaginal sonography or pathologic confirmation of gestational tissue from surgical procedures.

Parameters determined in both groups included age, day 3 FSH, number of antral follicles, number of ampoules of gonadotropins used; estradiol (E_2) level on the day of hCG administration, endometrial thickness (mm) on the day of hCG administration, number of dominant follicles, number of retrieved and fertilized oocytes, number of embryos transferred, clinical preg-

nancy rate, spontaneous abortion rate, and total delivery rate.

Results are presented as mean values $\pm$ standard deviation (SD). Comparisons between means among the study groups were performed using the Student's *t* test. Fisher's exact test was applied to compare the outcome of IVF between the two groups. A value of $P < 0.05$ was considered statistically significant.

RESULTS

The age, day 3 FSH, and number of antral follicles were not statistically significant between the two groups (Table I). There was no statistically significant difference in the number of ampoules of gonadotropins used, E_2 level, and endometrial thickness (mm) on the day of hCG administration, and number of dominant follicles between the groups (Table I). There was no difference in the number of retrieved oocytes, number of fertilized oocytes, and number of embryos transferred in either group (Table I). The clinical pregnancy rate and total delivery rate were not statistically significant between the patients who had a sonographically diffusely enlarged uterus without distinct uterine masses and the patients who had a normal uterus (Table II). The spontaneous abortion rate was significantly higher among the patients who had a sonographically diffusely enlarged uterus without distinct uterine masses than among the patients who had a normal uterus. The presence of a sonographically diffusely enlarged uterus without distinct uterine masses increased the odds of abortion 7.5-fold (95% confidence interval, 1.16–48.56; $P < 0.04$) (Table II).

DISCUSSION

The presence of a sonographically diffusely enlarged uterus without distinct uterine masses is a common finding in patients with diffuse adenomyosis. About 80% of diffuse adenomyosis uteri can be diagnosed by the criteria of sonographically diffusely enlarged uterus and a dishomogeneous area in the myometrium with indistinct margins and containing anechoic lacunae of varying diameter (1). However, multiple leiomyomas, coexisting adenomyosis and leiomyomas, or huge leiomyomas also are possible.

Few data are available on the outcome of IVF in patients with a sonographically diffusely enlarged uterus without distinct uterine masses. A previous report showed that pregnant women with adenomyosis

Table I. Cycle Profiles of the IVF Program Between Patients with a Sonographically Diffusely Enlarged Uterus Without Distinct Uterine Masses and Patients with a Normal Uterus^a

Variable	Sonographically diffusely enlarged uterus without distinct uterine masses		P
	Present (n = 19)	Absent (n = 144)	
Age (year)	36.0 ± 2.6	35.4 ± 2.8	NS ^b
Day 3 FSH (mIU/ml)	7.2 ± 2.3	6.5 ± 2.3	NS
No. of antral follicles	8.7 ± 7.1	11.4 ± 7.3	NS
No. of ampoules of gonadotropins used	40.6 ± 14.0	35.0 ± 16.2	NS
E ₂ level (pg/ml) on day of hCG administration	1187 ± 1100	1613 ± 1093	NS
Endometrial thickness (mm) on day of hCG administration	10.0 ± 2.0	10.5 ± 3.4	NS
No. of dominant follicles	7.9 ± 2.4	8.7 ± 3.8	NS
No. of oocytes retrieved	6.6 ± 3.2	7.2 ± 2.1	NS
No. of fertilized oocytes	5.3 ± 2.0	6.2 ± 4.1	NS
No. of embryos transferred	3.8 ± 1.2	4.2 ± 1.9	NS

^a Data are mean ± SD.^b Not significant.

uteri have a higher incidence of hemorrhage with spontaneous abortion, cervical, tubal, or intramural ectopic pregnancy, placenta previa, uterine rupture on manual curettage or in labor, and uterine atony (8).

We found that patients with a sonographically diffusely enlarged uterus without distinct uterine masses did not influence the ovarian response of controlled ovarian hyperstimulation, number of retrieved oocytes and transferred embryos, clinical pregnancy rate, and total delivery rate with respect to the age-controlled group. However, a high spontaneous abortion rate was found in patients having a sonographical pattern of diffusely enlarged uterus without distinct uterine masses undergoing IVF. The risk was 7.5-fold higher than in those who did not bear the sonographical pattern.

The adverse effect of a sonographically diffusely enlarged uterus without distinct uterine masses on the high spontaneous abortion rate may be explained by the similar mechanisms occurring in adenomyosis patients. Fedele *et al.* reported that 38.8% (7/18) of

patients who conceived after adenomyomectomy had spontaneous abortions, which is a higher rate than would be expected in a normal population (9). Olive *et al.* reported that 66.7% of patients with adenomyosis (12 of 18) aborted (2). Speculative theories about the etiology of spontaneous abortion in patients with adenomyosis include mechanical traction and distortion of the adenomyotic foci and uterotubal spasm caused by local prostaglandin released by ectopic endometrial implants. These implants localized in the myometrium could continue to irritate the uterus in early pregnancy, with the resulting uterine spasm sufficient to disrupt pregnancy and produce a spontaneous abortion (2).

In conclusion, patients with a sonographically diffusely enlarged uterus without distinct uterine masses are associated with a high spontaneous abortion rate in IVF program. Therefore, luteal support in such patients should be reinforced. However, the necessity of a conservative surgery to excise the lesion of a sonographically diffusely enlarged uterus without distinct uterine masses for the prevention of spontaneous abortion

Table II. Outcome of the IVF Program Between Patients with a Sonographically Diffusely Enlarged Uterus Without Distinct Uterine Masses and Patients with a Normal Uterus

Variable	Sonographically diffusely enlarged uterus without distinct uterine masses		P ^a	OR (95% CI) ^b
	Present (n = 19)	Absent (n = 144)		
Clinical pregnancies	6 (31.6%)	38 (26.4%)	0.594	1.29 (0.46–3.63)
Abortions	4 (66.7%)	8 (21.0%)	0.039	7.50 (1.16–48.56)
Deliveries (of total cases)	2 (10.5%)	36 (25.0%)	0.248	0.35 (0.08–1.60)

^a Fisher's exact test.^b Odds ratio (95% confidence interval).

remains undetermined. Further studies in a larger series of patients are needed to confirm these findings.

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