In Vitro Fertilization Treatment in Genital Tuberculosis

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Purpose: We describe our experience with in vitro fertilization (IVF) treatment in 13 women with histologically proven genital tuberculosis.

Methods: For IVF treatment the above patients had to meet two criteria: normal uterine cavity and functional ovaries.

Results: Six intrauterine pregnancies (28.6% success rate) were achieved after 21 IVF treatment cycles in 13 patients with histologically proven diagnoses of genital tuberculosis. This series represents a comparatively encouraging success rate, but these patients were selected carefully before committing them to IVF treatment.

Conclusions: IVF represents a useful treatment and improves the chances of fertility, in what was considered a desperate situation.

KEY WORDS: tuberculosis; infertility; in vitro fertilization.

INTRODUCTION

The incidence of genital tuberculosis (TB) is increasing in the Western world, because of the increasing migration from the Asian subcontinent and the emergence of strains of *Mycobacterium tuberculosis* resistant to anti-TB therapy. There are conflicting views on whether successful pregnancy may be expected after treatment of genital TB, with most authors considering the prognosis to be very poor (1–4).

Frydman *et al.* (1985) (5) first demonstrated the usefulness of in vitro fertilization (IVF) in the management of TB infertility but no further data have been published.

We describe our experience with IVF treatment in 13 women with histologically proven genital TB.

MATERIALS AND METHODS

During the period 1984 to 1993 at Hammersmith Hospital approximately 3000 patients underwent more than 5500 IVF treatment cycles. Thirteen patients with histologically proven genital TB were identified from the IVF register. The mean age of the patients was 33 years (range, 29–37 years), and the mean duration of infertility was 8.75 years (range, 6–20 years). Ten patients were complaining of primary and the remaining three of secondary infertility. Five of the patients were Caucasian in origin, seven were Asian, and the remainder were from the Middle East. The majority of them were born in the United Kingdom.

TB salpingitis was demonstrated histologically in 10 cases, endometrial biopsies were positive in 2 cases, and in the remaining case both the endometrium and the tube were affected. Hysterosalpingography was suggestive of genital TB in 8 cases (61%) according to the criteria of Klein *et al.* (6).

The primary affected site was the lung in five cases, the abdomen in two, the endometrium in two, and the fallopian tube in four. In four patients acid-fast bacilli were cultured from menstrual blood, the endometrium, or the hydrosalpinges. The hydrosalpinges for those patients were not removed and they did not conceive with IVF treatment.

All patients had triple chemotherapy for 18–24 months prior to referral. Six to twelve months following treatment they were allowed to have IVF done.

Care was taken to ensure that the uterine cavity was fully assessed and that all adhesions were carefully divided, prior to treatment. In this respect, hysterosalpingography and hysteroscopy are essential preliminary investigations and were used extensively. One hysteroscopic division of adhesions was performed. All patients had hormone profile, laparoscopy, vaginal ultrasonography, and sperm assessment performed prior to the IVF treatment.

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RESULTS

Twenty-one treatment cycles were performed. The superovulation protocol was buserelin/human menopausal gonadotropin (hMG) in 20 cycles and clomiphene citrate (CC)/hMG in the other cycle. Egg collections were performed under ultrasound control.

Four cycles were canceled due to poor superovulation, and 17 egg collections were performed. The average number of oocytes collected was 8.3 per puncture, and the fertilization rate was 55%. The average number of embryos available was 5.1. Embryos were available for transfer in 16 of the cycles. Two or three embryos were transferred per patient. The oocyte and embryo quality was similar to that of other patients without TB.

There were six intrauterine and no ectopic pregnancies in five (39%) of the patients. Four patients have delivered and the fifth had two missed abortions in the first trimester. The pregnancy rate was 35.2% (6/17) per puncture and 37.5% (6/16) per embryo transfer.

DISCUSSION

Widespread vaccination, antibiotic treatment, and improvement of socioeconomic conditions in the past 30 years have resulted in a considerable decrease in the frequency of TB in the Western world (7). Recently, however, the incidence of the disease has been rising and widespread resistance to isonizide has been documented. Also, the use of the polymerase chain reaction has been shown not only to improve diagnostic accuracy but also to detect resistance to rifampicin (4,8).

Genital TB is still rare in the United States (3,6), but it remains a problem in the developing countries. Figures as high as 10 to 15% have been reported among selected and unselected women subjected to endometrial biopsy for primary infertility in India (9).

In Saudi Arabia, where the economic background is similar to that in Western countries, the incidence of genital TB is much higher, at 0.45% of all gynecological admissions and 4.2% of those complaining of infertility (10). Third-world immigrants also demonstrate a higher incidence of genital TB compared with the indigenous populations of the host countries. North African immigrant women in France have the same pattern of infertility problems as native French women, the main difference being that genital TB occurred in 33% of them, compared with only 6% of the general population (11).

The prognosis of a successful pregnancy after treatment of genital TB is very poor. Falk *et al.* (3) reported that the chances of having a normal pregnancy are almost nil and the risk of an ectopic pregnancy is great. Schaefer (1) believes that pelvic TB that involves the peritoneal surface but not the mucosa does not impair reproductive function, whereas patients with mucosal involvement should be regarded as infertile, probably owing to scarring of the endometrium, which prevents implantation. These patients had no success with IVF. According to his review of more than 7000 cases of genital TB from the literature, it was possible to find only 31 full-term pregnancies in patients treated for genital TB when histologic or bacteriologic verification of the diagnosis was required (1). De-Vynck *et al.* (12) reported 13 pregnancies in 34 patients following anti-TB therapy. All the patients included in this study have histologically proven genital TB and have completed their full course of chemotherapy.

In our unit a systematic workup is done prior to committing a patient to IVF treatment. This includes a laparoscopy, a hysterosalpingogram, a vaginal scan, and a hysteroscopy if indicated. In cases of genital TB it is extremely important to assess the uterine cavity fully and divide any adhesions. In our experience hysterosalpingograms were suggestive of genital TB in eight cases (61%). The characteristic findings were sclerotic and brush border tubes. This compares favorably with the 9 of 20 (45%) reported by Frydman *et al.* (5). Hysteroscopic division of adhesions was performed in one patient but she did not become pregnant. Laparoscopy also confirmed that the remaining seven patients had tubal involvement with adhesions. Laparoscopy and hysteroscopy were used as supplementary methods to exclude patients.

It is generally agreed that acid-fast bacilli are difficult to isolate in culture. Cultures of menstrual blood are most useful and, in the series of Oosthuizen *et al.* (13), were positive in 69.9% of patients with positive cultures. In our series they were positively identified in four cases. Patients with positive cultures did not conceive with IVF treatment.

In cases of tubal disease it has been found that macro- and microsurgical procedures very rarely lead to a successful intrauterine pregnancy, while they significantly increase the chances of an ectopic pregnancy (3). In contrast, Tumanov and Kochorova (14) advocate selective use of microsurgical techniques and achieved a 9% improvement in pregnancy rate. Winston and Margara (15) reported microsurgical repair

of the tubes in five patients with genital TB and found two normal pregnancies.

Frydman *et al.* (5) reported a pregnancy rate of 16.3% per puncture and 25% per transfer following IVF treatment of patients with tuberculous infertility. Superovulation with buserelin/hMG versus CC/hMG and transvaginal versus laparoscopic oocyte recovery as well as the general improvement in embryologic standards may account for the higher success rate in our study.

We conclude that IVF treatment probably represents the most successful treatment for patients with genital TB, provided that these patients have a normal uterine cavity and functional ovaries. Patients with positive cultures should not be allowed to begin IVF treatment.

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