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An Experience of Intravaginal Auto Lymphocyte Therapy in Treatment of Female Patients with Infertility: A Case Report

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Case Study

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ABSTRACT

Aim: Application of a new method – intravaginal auto lymphocyte therapy in treatment of female infertility.

Place and Duration of Study: I.M. Sechenov, First Moscow State Medical University, the study was performed in 2010.

Results: A case report concerning treatment of a female patient with infertility by use of a new method of intravaginal administration of auto lymphocytes is presented. To prepare the patient to infertility treatment with help of intravaginal fertilization (IVF), 5 performances of intravaginal auto lymphocyte therapy were made. A pregnancy resulted simultaneously after the treatment course and finished by operative childbirth.

Conclusion: In the case presented here the method of intravaginal auto lymphocyte therapy demonstrated its efficiency in treatment of infertility. We hope that in immediate future this method will provide us with a possibility to improve female infertility treatment results.

Keywords: Infertility; IVF; auto lymphocyte therapy; lymphocyte therapy.

1. INTRODUCTION

Infertility in marriage is one of the most actual problems possessing social and economic importance. According to results of epidemiological investigations, the frequency of infertility in marriage in many countries in the world varies from 8 to 29% (Araoye, 2003) and in the present time there is no tendency for decreasing. Thus, development and introduction into clinical practice of new methods of infertility treatment represent an actual problem of the modern medicine.

More often the disorders in female reproductive sphere are linked with endocrine pathology of gynecological diseases. However, in some cases the reproductive function even in cure of above mentioned diseases is not restored. Further studies demonstrated that immune system participates also in regulation of the reproductive function (Fujiwara et al., 2006). Takabatake et al. (1997) showed that immune cells may cause differentiation of the endometrium at preimplantation stage, thus preparing it to embryo implantation. Immune cell intracellular interactions in endometrium of a mother determine predominantly implantation processes, degree of trophoblast adhesion and invasion and as a consequence a normal development of pregnancy, while different pathological processes in the endometrium (defect secretory transformation, inflammation) may lead to implantation defects (Klentzeris, 1999). Works appeared during last years describe application of autologic immunocompetent cells (mononuclears) during execution of extracorporal impregnation in order to improve results of embryo implantation in female patients with many unsuccessful attempts of IVF. According to results of these studies intrauterine administration of mononuclear cells, activated in vitro by pharmacological preparation – human chorionic gonadotropin (HCG) simultaneously with fertilized oocyte sufficiently increased percent of positive results of the IVF results (Fujiwara and Yoshioka, 2002; Nakayama et al., 2002).

In the present article a clinical case of usage of a new method of treatment related to methods of extracorporal pharmacological therapy is presented – intravaginal auto lymphocyte therapy. The method was used in the infertile patient in order to prepare her to the program of intravaginal fertilization and embryo transfer (IVF and ET). After the treatment course a pregnancy came simultaneously and was completed by operative childbirth.

2. CASE PRESENTATION

A female patient of 40 years old appealed to out clinics with complaints at irregular menstrual cycle and absence of pregnancy during 18 years of regular relations.

Anamnesis: Menstruation from 13 years old, during 5 days, every other 25-40 days, sexual relations from 18 years old. In 1991 after stimulation by clomiphen a pregnancy onset took place, interrupted by spontaneous abortion at term 11-12 weeks. Abrasiocavi uteri were made, complicated by acute endometritis. In 1999 with diagnosis: «Secondary infertility. Polycystic ovarian syndrom», she was placed to division of operative gynecology, where laparoscopy and wedge-like resection of ovaries were made. There was no pregnancy onset after the treatment.

Infection was not detected by PCR diagnostics during laboratory and instrument investigation of the patient. Acytogram of cervical channel and uterus cervix was in norm range. USI of organs in small pelvis at 7-th day of the menstrual cycle: a uterus 48x35x49 mm, the cavity not deformed. M-echo 5 mm, endometrium with hyperechogenic inclusions.

Right ovary in volume of 10,9 cm³, altered, polycysts. Left ovary in volume of 18,0 cm³, altered, polycysts.

Conclusion: USI-picture of polycystic ovaries, suspicion for chronic endometritis. In hysterosalpingography no disruption of uterus tubes passage from both sides were detected.

In the first phase of the cycle the patient was subjected to hysteroscopy with biopsy of endometrium. Visually a swollen endometrium with fibrin layers is observed. Mucus demonstrates expressed vessel picture with elevated hemorrhage properties. During histological investigation of biopate of endometrium there was a certain lymphocyte and leucocyte infiltration, a stroma swelling, sites of endometrium necrosis were observed.

In investigation of hormonal status an elevation of testosterone level (51,13 pmole/l, in norm 3,5-29,5 pmole/l), LG\FSG= 2,64 (Table 1) are revealed. In immunogram: an absolute amount of CD4+ cells is decreased, also relative and absolute amounts of B-lymphocytes (CD19+) are decreased, in the same time the relative content of natural killers (CD16+) is increased and T-leuco-lymphocyte index (Table 2) is elevated. Results of the husband investigation were under norm, conclusion on spermogram – normzoospermia.

Table 1. Results of investigation for hormones at 3rd day of a menstrual cycle

Index	Result	Norm
Follicle-stimulating hormone	5,21 mE/ml	1,2-9 mE/ml
Luteinizing hormone	13,8 ME/ml	0-14,7 ME/ml
Estradiol	112,9 pg/ml	18,9-246,7 pg/ml
Prolactin	198 mE/l	95-700 mE/l
Progesterone	0,321ng/ml	0-1,13ng/ml
Testosterone	51,13 pmole/l	3,5-29,5pmole/l
Digidroepiandrosteron	202 pg/ml	24-450 pg/ml
17-OH- progesterone	0,2 ng/ml	0,2-1,2 ng/ml

The next diagnosis was made, taking into account the anamnesis and investigation results: Secondary infertility, chronic endometritis and Polycystic ovarian syndrome.

Taking into account the age of the patient, intravaginal fertilization was recommended as a treatment method. Under preparation to IVF it was decided to perform a course of intravaginal auto lymphocyte therapy in combination with receiving of duphaston. The method is based on use of own blood cells – auto lymphocytes, activated in vitro by an immunomodulator - immunofan. Then washed activated viable lymphocytes are returned into the organism, i.e. into the natural environment where they realize their functions. In that, a local impact on immunocompetent cells of vagina and uterus cervix takes place, and also we receive a possibility to mediated influence on the uterus corpus and its appendages, assisting regeneration and normalization of endometrium functions Suspension of auto lymphocytes does not contain medicinal preparations, so this method does not cause side effects.

Table 2. Results of immune status investigation

Index		Norm	Result
Leukocytes	abs.	4 000-9 000	6 300
Lymphocytes	%	19-37	19
CD 3 ⁺ (T – lymphocyte)	abs.	1 200 - 3 000	1 197
	%	55-80	72,2
CD 4 ⁺ (T – helper)	abs.	800-2 200	864
	%	31-49	44,7
CD 8 ⁺ (T – cytotoxic lymphocyte)	abs.	600 - 1 600	535
	%	19-37	33,5
CD4 ⁺ /CD8 ⁺ index	abs.	300-800	400
		1,0-2,5	1,33
CD 19 ⁺ (B – lymphocyte)	%	5-19	3,2
	abs.	100-500	38
CD 16 ⁺ (natural killers)	%	6-20	22,5
	abs.	150-550	269
D – neutrophils	%	20-64	52
T- leucocyte/lymphocyte Index		4-7	7.29
Immunoglobulins mg%	A	100 - 350	280
	G	900 – 1 800	1560
	M	80-250	120

The patient was subjected to 5 procedures of intravaginal auto lymphocyte therapy in an interval of 7 days, duration of one procedure was 1 hour. After completion of the treatment course during 4 months the patient became spontaneously pregnant.

3. DISCUSSION

Any changes in the immune system are accompanied by dysfunctions of reproductive process that may cause infertility and miscarriages (Sidelnikova, 2002). Presence of any immune disorders may be a serious reason of oocyte impregnation defects, disruption of embryo implantation and loss of pregnancy. In this connection, intravaginal auto lymphocyte therapy is a one of alternative methods of influence on local immunity that does not cause negative influence on general immune system.

A mechanism of this type of treatment is still unknown and requires further investigation. We suppose that the reason of infertility may be dysfunction of local immunity and presence of chronic inflammatory process in the endometrium, than leads in both cases to disruption of receptor properties of the endometrium and the embryo implantation disorder. The intravaginal auto lymphocyte therapy influences positively on normalization of immune response processes as well as course of inflammatory process.

It is known, that the chronic endometritis not infrequently acts as one of infertility factors and unsuccessful applications of IVF (Kasius et al., 2011). According to data of Gazazian et al., (1998), a chronic endometritis was revealed in 25,2 % of women, suffering from reproductive function disorders. In this a secondary infertility were revealed in more than every other patient - 58,3%. Studies during last years reveal significant changes of immunity parameters in female patients with chronic endometritis in the form of activation of cellular and humoralproinflammatory reactions, lymphocyte infiltration of endometrium, local elevation of T-lymphocytes, NK-cells (natural killers), macrophages, IgM, IgA, IgG titers (Gazazian and Khardikov, 2010).

Alike morphological alterations in endometrium, disruption of immune reactions at local level may act as starting mechanisms of impregnated oocyte rejection and destruction. A negative role of activated natural killers — NK-cells in the development of immune infertility is discussed (Matsubayash et al., 2001). Natural killers — population of lymphocytes, performing a wide set of biological functions on regulation of cell differentiation and elimination of genetically defect cells and also cells infected by pathogens without preliminary immunization (Sepiashvili and Balmasova, 2006). In norm there are all types of immunocompetent cells in endometrium, but NK-cells constitute the biggest population of lymphocytes (up to 70%). Predominantly, NK-cells possess low cytolytic activity, but in certain conditions they are activated (CD56+ CD16+) and acquire ability to destroy cells of developing trophoblast (Faridi et al., 2009; Vaccao et al., 2008). It is shown, that elevation of NK-activity is associated with infertility and failure in IVF results (Nerivals et al., 2001).

In some cases immunological alterations in endometrium (lymphocyte infiltration, elevated concentration of plasmatic cells and immunoglobulins, changes of ration of T-lymphocyte's cytokines of 1-st and 2-nd types etc.) may serve as independent reason of infertility and miscarriages. Thus, some authors consider that introduction of preparations with immunomodulating activity into complex of treatment procedures for patients with chronic inflammatory diseases of organs of small pelvis and infertility sufficiently accelerates processes of tissue regeneration, normalization of menstrual and reproductive function (Shurshalina, 2007). The method of auto lymphocyte therapy influences on local immunity, but do not mean introduction of immunomodulating preparations into the organism. Due to this, the method is safe and has no side effects.

4. CONCLUSION

In this clinical case the intravaginal auto lymphocyte therapy method was effective in treatment of the infertile female patient. We hope in future to increase efficiency of treatment of infertile female patients as in natural cycle as well as in IVF and ET program improving methods of auto lymphocytes cultivation and their stimulation by various pharmacological preparations and also developing new methods and ways of auto lymphocytes administration. Although the precise mechanism of the action is still unknown, further development of this approach has very great perspectives.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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