



Case Report

Sat-Therapy Treatment in IVF Patient: A Case Report

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Abstract

31-year-old caucasian woman with history of primary infertility and reduced ovarian reserve. Blood tests revealed a significant depletion of circulating NK. The patient underwent two IVF attempts that failed. After SAT Therapy (Sero-Homeotherapy A specific Tissue) cycles, she had a spontaneous pregnancy. Immune system plays a very important role in the fertilisation and attachment of the embryo. In the early stages of pregnancy, in fact, maternal blood is redirected to the placenta through remodeling the uterine spiral arteries. NK cells have a fundamental role in the initial stages of this process. Immunodepletion of these cells causes a reduced supply of oxygen to the placenta in early pregnancy, thereby interfering with fertility and causing dramatic changes in the placental structure. This can lead to pregnancy failures. Sat-therapy is a new biological branch of homeopathic medicine that use glycoprotein fractions of animal origin. It can be used to restore the correct physiological metabolism of tissues and organs damaged by disease and aging. In this case, SAT therapy was effective in reproducing proper functioning of the immune system, allowing the patient to have pregnancy without undergoing further assisted reproduction techniques.

Keywords: Natural killer; Spontaneous pregnancy; Ovarian stimulation; IVF; SAT therapy

Introduction

Natural Killer Cells

Natural killer (NK) cells are lymphocytes of the innate immune system that are best known for their ability to mediate cytotoxicity and produce cytokines after the ligation of germline encoded activation receptors [1] These cells are best appreciated for innate defense against viral infections and in tumor cells surveillance, but are also increasingly recognized for participating in immunoregulation, coordination of immunity and modulating autoreactivity. After activation, NK cells are capable of three main functions to participate in immune defense. The first and best characterized is the ability to mediate contact dependent killing of target cells. The second function of NK cells is the production of soluble factors to promote direct anti-disease effects as well as further induce or regulate immunity. These include a wide variety of cytokines, chemokines, and other regulators. The third function is that of promoting and regulating immunity through contact dependent costimulatory and regulatory mechanisms.

NK Cells and Pregnancy

A key event for successful pregnancy is the redirection of maternal blood to the placenta. This task is accomplished through remodeling the uterine spiral arteries (the vessels that supply the placenta with maternal blood) from low-flow vessels into high capacity conduits [2]. Remodeled spiral arteries can carry an enhanced and consistent supply of maternal blood to the placenta, thereby ensuring that the fetus obtains sufficient nutrients and gases to sustain his growth and development. Two specialized cell types are thought to contribute to spiral artery remodeling: invasive trophoblast cells emanating from the placenta and maternal immune cells belonging to NK-cell lineage [3]. Trophoblast cells adjacent to the decidua develop invasive properties. These “invasive” trophoblast cells dissociate from the placenta and infiltrate the decidua, where they aggregate around and within the spiral arteries causing displacement of the native endothelium, and destruction of the surrounding elastic lamina and smooth muscle coat surrounding the vessels [2,4]. Consequently, the spiral arteries become flaccid, distended, trophoblast-lined vessels that carry a large and unimpeded supply of maternal blood to the placenta. Prior to the onset of trophoblast infiltration, a contingent of NK cells accumulates within the decidua where

they comprise approximately 70% of all leukocytes in the uterus during early pregnancy [5]. The accumulation of NK cells within the uterus contrasts with other lymphocytes, which are generally excluded from the implantation site. These uterine NK cells are phenotypically and functionally distinct from most NK cells that reside within other tissues. The number of uterine NK cells dwindles around the time that trophoblast cells begin to invade into the uterus, and they are scarce by term [6,7]. The function of uterine NK cells is not clear. The prevailing stance is that these cells help to build a healthy placenta [8]. Pregnant mice genetically devoid of NK cells exhibit spiral arteries with narrow lumens, intact tunica media, and swollen endothelial cells, implying that NK cells are vital for guaranteeing correct spiral artery remodeling in this species [9]. In line with the importance of NK cells for facilitating placental blood flow, compromised fetal growth has been observed in mice lacking NK cells and in mice with reduced NK-cell function [10-12]. NK cells appear to initiate angiogenesis and at least a partial spiral artery remodeling in humans and rats as well, since dilation and medial disorganization of spiral arteries is evident prior to the arrival of invasive trophoblast cells [13,14]. Consistent with a role for NK cells in the initial stages of spiral artery development, their immunodepletion causes reduced oxygen delivery to the placenta early in pregnancy and causes dramatic alterations to placental structure.

SAT Therapy

SAT therapy is a therapeutic method resulting from the studies of Dr. Jean Thomas (1902-1977) that uses SAT derivatives, homeopathic medicines containing glycoprotein fractions diluted and dynamized in DH4 (10- 4 gr / ml). The task of SAT therapy is to stimulate body's defenses and promote tissue renewal. To achieve this, it uses SAT derivatives (anti-tissue serum hemoderivatives) which contain specific antibodies produced by mammals. These remedies are purified, diluted and dynamized according to homeopathic practice. The diluted preparations, called Serolab, can be taken by different routes of administration: oral, sub-lingual or rectal. Serolabs can be administered also with micro-injections on the skin using Chinese acupuncture points. SAT therapy is characterized by an extreme therapeutic precision, without repercussions on other levels of the body. It provides a non-toxic corrective action so it can be used for long periods without ever incurring iatrogenic or accumulation or habituation problems. These features make SAT therapy an innovative and reliable therapeutic method. It can be used as the only therapeutic device, or as a basic support for other methods of treatment. SAT therapy is essential in all situations in which the body has lost the ability to correct its malfunctions and to repair the injuries that have occurred. It is evident that a destroyed tissue will not be able to respond to the treatment. Therapeutic schemes last 4 weeks: 3 of treatment and 1 of rest. This therapy can act on many systems, like the urogenital system where it can be used to treat premenstrual

syndrome, dysmenorrhea, vaginitis, fibroids, adenoma and cystic disease of the sinuses, inflammations of the urinary tract, diseases of the kidneys, menopause, andropause, anti-aging therapy.

Case Report

31-year-old Caucasian woman with history of primary infertility with reduced ovarian reserve (Anti-Mullerian Hormone, AMH = 0.85 ng / ml). During investigations carried out for the in vitro fertilization (IVF) cycle, emerged a Lupus Anticoagulant (LAC) positivity, and Anti-Cardiolipin Antibodies (ACA) IgM and IgG were found positive (26.7 MPL/ml and 87.6 GPL/ml). Methylene tetrahydrofolate reductase gene (MTHFR) A1298C was mutated in homozygosity. Genetic tests were negative. Blood test showed an increase of T Helper lymphocytes with CD4 / CD8 ratio at the upper limits of the reference ranges (1.89) and significant reduction of circulating Natural Killer lymphocytes (167 / μ l). Blood group was 0 Rh Negative. In anamnesis, familiarity for breast cancer (mother, aunt and grandmother were affected), but the recent breast ultrasound of the patient was normal. Pap test, colposcopy, transvaginal pelvic ultrasound, and hysteroscopy were negative. Male semen was normospermic. After a diagnosis of primary infertility, in January 2018, the patient underwent the first ovarian combined stimulation protocol with GnRH analogue hormone (Triptorelin; Decapeptyl, Ipsen, Milan, Italy) 0.1 mg/day from the first day of the cycle until hCG day [15-21]. Ovarian stimulation started with recombinant FSH (rFSH; Puregon, MERCK, Italy) 150 IU/day and 150 IU/day of human menopausal gonadotropin (hMG, Meropur, Ferring, Italy) from the second day of cycle until hCG day. After 6 days of stimulation, the endometrial thickness was 8 mm, serum estradiol 286 ng / L, serum LH 4.8 U / L and serum progesterone 0.33 ng / ml. At twelve day of cycle, the patient presented: endometrial thickness 15 mm, serum estradiol 1786 ng / L, serum LH 4.8 U / L and serum progesterone 1.22 ng / ml. Final oocyte maturation was triggered by the administration of 10000 IU of human chorionic gonadotropin (hCG; Gonasi HP, IBSA, Switzerland) when at least half of the total follicles were 18 mm in diameter. Oocyte retrieval was performed 36 h after hCG administration. Nine oocytes were recovered: eight in metaphase II and one in metaphase I. Mature metaphase II oocytes were inseminated by intracytoplasmic sperm injection (ICSI).

Oocytes quality was very poor. One oocyte did not survive 24 hours, five stopped their growth at day 5 and two reached the blastocyst stage (one grade A and one grade D). Ultrasound guided embryo transfer was performed at the stage of blastocyst [22,23]. From the day after oocytes retrieval and until pregnancy test, luteal phase was sustained by Progesterone 50 mg/ day (Prontogest, IBSA, Switzerland), Prednisone 10 mg day (Deltacortene, Bruno Farmaceutici, Italy) and Enoxaparin 4000IU day (Clexane 4000, Sanofi, France). However, the patient does not get pregnant. In April 2018, the patient underwent a second attempt [15-21] of

ovarian stimulation using GnRH analogue hormone (Triptorelin; Decapeptyl, Ipsen, Milan, Italy) 0.1 mg/day from the first day of the cycle. Ovarian stimulation began with the administration of gonadotropins, from the second day of the cycle, while triptorelin administration was continued up to hCG day. The patients received recombinant FSH (rFSH; Gonal-F 900, Merck Serono, Italy) starting with the dosage of 150 IU/day from the second day of the cycle simultaneously with 200 IU/day of human menopausal gonadotropin (hMG, Meropur, Ferring, Italy).

After 6 days of stimulation the patient presented: endometrial thickness 9.8 mm, serum estradiol 760 ng / L, serum LH 5.1 U / L, serum progesterone 0.18 ng / ml. Final oocyte maturation was triggered by the administration of 10000 IU of human chorionic gonadotropin (hCG; Gonasi HP, IBSA, Switzerland) when at least half of the total follicles were 18 mm in diameter. Oocyte retrieval was performed 36 h after hCG administration, and the retrieved oocytes were denuded from their cumulus cell and were assessed for their maturity. Eight oocytes have been retrieved: seven in metaphase II e one in metaphase I. Mature metaphase II oocytes were inseminated by intracytoplasmic sperm injection (ICSI) but none of them reached the blastocyst stage. Therefore, the embryo transfer is not carried out, the physician decided for next IVF attempt with Egg donation. Before treatment, the patient underwent a Sat-Therapy treatment in association with folic acid and protease inhibitor for a total of 9 weeks. The patient was subjected to a first Sat-therapy cycle with Emonc-Tr 4dh (Serolab, Laboratorio Sodini, Italy) 0,5ml, Sre 4dh (Serolab, Laboratorio Sodini, Italy) 0,5ml, Sym-To 4dh (Serolab, Laboratorio Sodini, Italy) 0,5ml, Foe 4dh (Serolab, Laboratorio Sodini, Italy) 0,5ml, Neuglan-F 4dh (Serolab, Laboratorio Sodini, Italy) 0,5ml. After that, the patient underwent to a second cycle with Emonc-Tr 4dh (Serolab, Laboratorio Sodini, Italy) 0,5ml, Sym-To 4dh (Serolab, Laboratorio Sodini, Italy) 0,5ml, Foe 4dh (Serolab, Laboratorio Sodini, Italy) 0,5ml, Neuglan-F 4dh (Serolab, Laboratorio Sodini, Italy) 0,5ml. The third cycle consisted in Emonc-Tr 4dh (Serolab, Laboratorio Sodini, Italy) 0,5ml, Dien-Ph 4dh (Serolab, Laboratorio Sodini, Italy) 0,5 ml, Hevare 4 dh (Serolab, Laboratorio Sodini, Italy) suppository.

Emonc-Tr 4dh balances global functional of the various excretory organs of the body. It works by restoring the extracellular information exchange between the intestine, liver, kidney, pancreas, endothelial reticular system, gallbladder, lung, skin, lymphatic ganglia. It can be used for metabolic diseases, in the accompaniment of complex therapies that generate side effects; it restores the organic response capacity and modulates the metabolism of the organs indicated above. Sym-To finds its antigenic imprinting in anterior and posterior hypothalamus and Dien-Ph in diencephalon. They are used for modulating the non-specific endocrine regulation activity and the ortho - and parasympatic activity. Dien-Ph finds use in neurovegetative dystonias, psychosomatic manifestations,

functional disorders, depression, anxiety, and sleep disturbances. Neuglan-F finds antigenic imprinting in the ovaries, anterior pituitary, diencephalon, thyroid, adrenal gland and is the great modulator of the activity of the female neuroendocrine axis [24] . At the end of the therapeutic protocol of SAT therapy, increasing serum concentration of beta hCG and the presence of intrauterine gestational sac demonstrated pregnancy.

Patient Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Discussion

The immune system plays a very important role in the placental structure and attachment of the embryo. One of the fundamental mechanisms of a successful pregnancy is the redirection of maternal blood to the placenta through remodeling the uterine spiral arteries [2]. NK cells have a fundamental role in this stage and their immunodepletion causes reduced oxygen delivery to the placenta early in pregnancy. NK-cell deficiency can interfere with fertility and during pregnancy causes dramatic alterations to placental structure that can lead to pregnancy failures [25]. In this case report, a 31- year-old Caucasian woman had an history of primary infertility and presented an important reduction of circulating NK cells. After two failed IVF attempts, she underwent SAT therapy cycles.

In a similar case report of Nocchioli et al. [24], SAT therapy was used to resolve the premenstrual syndrome (PMS). A 34-year-old woman with severe premenstrual syndrome which caused mood swings and aggression. She reported symptoms in the week preceding menstruation with a worsening change in mood which, from being serene and friendly, became aggressive and intolerant. The patient underwent SAT therapy after failed attempts with oral contraceptives, magnesium, and progesterone supplementation. The therapeutic scheme included three weeks of therapy and one week of rest, to be repeated twice. At the end of the first two months of treatment, the patient reported a marked improvement in premenstrual symptoms with absence of aggression and personality changes. Although the real etiology of premenstrual syndrome is unknown, the proposed treatment had a positive effect on the patient, with the remission of the symptoms and maintenance of well-being throughout the follow-up period. The neuroendocrine modulation exercised by SAT therapy played a leading role also on the serotonin pathways influenced by estrogen and progesterone in people with PMS [25]. Similarly, in this case report, SAT therapy helped to restore the immune response and the neuroendocrine axis allowing the patient to have pregnancy without further assisted reproduction techniques. In this case, SAT

therapy played a fundamental role in the recovery of the patient's well-being continuing its effects beyond the administration and throughout the follow-up period.

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Author's roles

A. Pacchiarotti is responsible of study design and critical discussion; L. Forte provided her clinical knowledge regarding SAT therapy; C. Sangiuliano, V. Berlinghieri and C. Vallone drafted the manuscript; The authors declare that the manuscript submitted is unpublished, original and is not under review with other publisher.

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