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Use of Blood Mononuclear Cells Autologous Fraction for Treatment of Menstrual Disorders (Case Report)

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ABSTRACT

The aim of our work was to investigate the effectiveness of circulating SC in the blood mononuclear fraction to restore normal functioning of the human ovaries.

AH270 patient complained to the clinic about an irregular menstrual cycle in the last 6 months (duration of the menstrual cycle from 38 to 60 days). On day 10 of the menstrual cycle, under general anesthesia, 2 ml of a solution containing a fraction of native nucleus-containing cells isolated from a pool of peripheral blood was administered transvaginally to the right and left ovaries. Microscopic examination of these cells showed that the obtained fraction contains polymorphic nucleus-containing cells of different sizes and high viability, which was 95-98%.

After 2 months, the patient came for a follow-up examination, during which an ultrasound of the pelvic organs was performed, as well as laboratory diagnostics of blood tests for AMH and FSH levels. Were taken according to the results of ultrasound of the pelvic organs, the following changes were observed - in the right and left ovaries there were 2 antral follicles in each, up to 3 mm in diameter. The duration of the menstrual cycle after the introduction of stem cells has decreased to 30-35 days. Thus, it is shown that the pool of nuclear-containing peripheral blood cells, which contains circulating progenitors and stem cells, has a powerful regenerative effect with concentrated topical administration, which in this case led to a full functional recovery of the ovaries and normalization of the menstrual cycle.

Keywords

Menstrual cycle, Ovarian follicular cycle, Donor eggs, Blood tests.

Introduction

The menstrual cycle of the female body is regulated by many factors. Irregularity of the menstrual cycle can be caused by disturbance in any of these several factors, thus it is hard to identify the pathophysiology of each problem. Correction by traditional methods is carried out with the use of hormone therapy and requires constant monitoring to achieve the effect and its subsequent maintenance. In addition, such treatment is often ineffective in terms of restoring fertility and patients need donor eggs.

The use of SC is a new approach in the treatment of this pathology, which is fundamentally different from the existing ones in that the cellular material is not a drug with a stable chemical composition, but instead is a living population of cells capable of receiving micro-environmental signals and synthesizing necessary substances. [1,2].

The link between the MSCs of the adult body and the ovarian follicular cycle has been confirmed by many researchers. To be more specific, studies on BMSC are quite popular and show positive results. It has been shown that such cells can stimulate the development of follicles from some types of ovarian stromal cells, or even form follicles from circulating germ cells [3,4].

As a source of cellular material for this type of treatment, the most promising is the use of their own SC, because it does not raise the issue of biosafety, compatibility, and ethical issues. Most often, bone marrow or adipose tissue is used to obtain stem and progenitor cells of the adult body [1,5]. In both cases, it is a traumatic procedure that requires surgery. The aim of our study was to investigate the effectiveness of circulating stem and progenitor cells in the blood mononuclear fraction to restore normal functioning of the human ovaries.

Materials and Methods

Obtaining the cell fraction: The patient's venous blood (200 ml) was collected, and heparin (2500 IU per 100 ml of blood) was added as an anticoagulant. The fraction of nucleated cells was isolated in a density gradient of "Isolate Irvine Scientific".

The resulting cell pellet was examined with a light microscope, the total number of cells and the percentage of living were counted using a Makler's chamber after staining with trypan blue. After that, the cells were concentrated in 2 portions of 2 ml by centrifugation (2000 about 10 min).

Intraovarian administration: Immediately after receiving the cell fraction, it was administered to the patient transvaginally in both ovaries under general anesthesia.

Examination: Ultrasound of the pelvic organs was made on Roche Cobas 6000 US machine. Level of FSH, AMH, Estradiol was controlled during all period of treatment.

Results

The patient, 42 years old, complained to the clinic about an irregular menstrual cycle in the last 6 months (duration of the menstrual cycle from 38 to 60 days). From the anamnesis it was known that the patient's menarche was at the age of 13, she had regular cycle (28-30 days) and 2 pregnancies that ended in physiological normal vaginal delivery. Laboratory test data didn't show any significant features (FSH - 62 mIU / ml, Estradiol - 150 pg / mL, AMH - 0.1 ng / ml). Ultrasound of the pelvic organs (Figure 1) showed signs of the first phase of the menstrual cycle (endometrial thickness - 4 mm, the number of antral follicles in the right ovary - 2 (2 mm each), in the left - 1 (3 mm)).

On day 10 of the menstrual cycle, under general anesthesia, 2 ml of a solution containing a fraction of native nucleus-containing cells isolated from a pool of peripheral blood was administered transvaginally to the right and left ovaries.

Microscopic examination of these cells showed that the obtained fraction contains polymorphic nucleus-containing cells of different sizes (Figure 2) and high viability, which was 95-98%.

Figure 1: Right ovary transvaginal scanning, one antral follicle visualized.

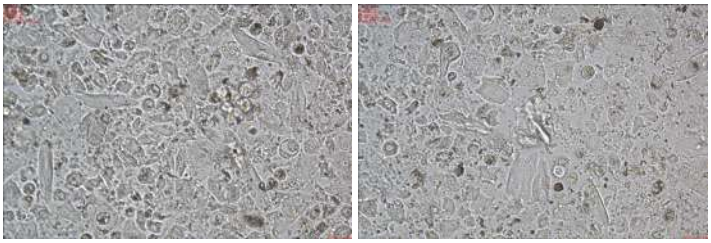

Figure 2: Concentrated fraction of blood mononuclears before injection. Living not-stained cells. X 200.

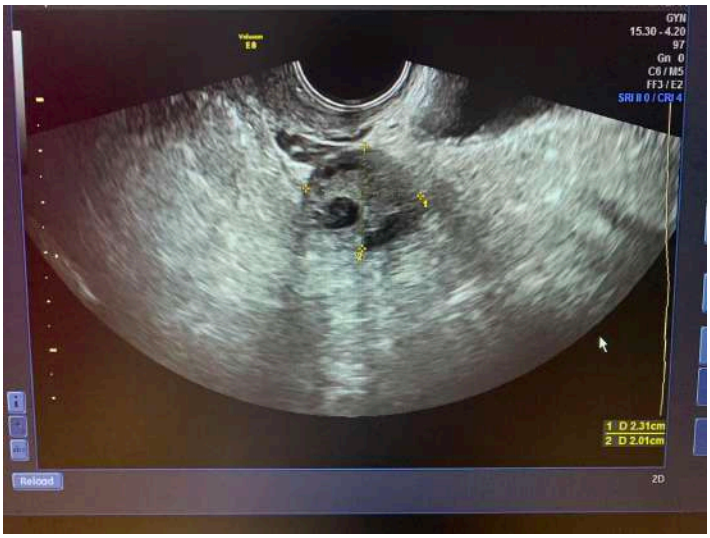

Figure 3: Right ovary transvaginal scanning, three antral follicle and the heterogeneous area (probably the site of the stem cells injection) visualized.

After 2 months, the patient came for a follow-up examination, during which ultrasound of the pelvic organs was performed, as well as laboratory diagnosis of blood tests for AMH and FSH levels. According to the results of pelvic ultrasound (Figure 3),

there were the following changes - in the right and left ovaries there were 2 antral follicles in each, up to 3 mm in diameter, blood FSH level - 50 mIU / ml, AMH level - 0.8 ng / ml. The duration of the menstrual cycle after the introduction of stem cells was 35 days, and the next - 30 days.

Discussion

The study of the relationship between the circulation of BMSC and follicle formation in the ovaries continues since the beginning of 2000. The effectiveness of their transplantation has been confirmed by numerous animal experiments and clinical studies, for example, in patients with Fanconi anemia [1-3,5,6].

According to the literature, it is known that among the pool of circulating nuclear-containing cells of peripheral blood there are progenitor and stem cells, in particular CD-105 positive MSCs. Recently, this pool of cells has received much attention as a mobile regenerative potential of the adult organism [7,8]. It is believed that this heterogeneous population is of bone marrow origin, it even contains pluripotent cells [1,2,5,7-9]. It is proved that their number increases during exercise and pathological conditions of various etiologies. Currently, studies on the clinical use of this fraction of cells, in particular in gynecology [1,2,5,7-9].

One of the probable mechanisms of action of BMSC is the expression and synthesis of trophic factors. Thus, the association between the presence of FGF-2 and the restoration of impaired expression of ovarian markers has been experimentally proven [5]. The presence of FGF-2 receptors in early follicles has been shown, and this protein has been shown to play an important role in estrogen production.

In addition, BMSC, including in the circulating pool, synthesizes high levels of IGF-1, TGF β1 and VEGF. The result of their influence is an increase in the proliferative activity of cells at the injection site, improved vascularization and subsequent structural and functional regeneration [10]. In addition, there are bolder hypotheses regarding the formation of follicles from circulating stem cells and germinal progenitors derived from BMSC [4].

Conclusion

Undoubtedly, this method of treatment of functional ovarian disorders has a right to exist. Some successful results, both ours and other researchers, require detailed analysis to determine the clinical signs of follicular failure, in which this method of correction will be most effective.

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