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Hyperhomocysteinemia: The Nature of Morphological Changes in Fetal Loss

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Abstract: The article provides data on the results of a morphological study of the early postabortem endometrium of women with hyperhomocysteinemia in the early stages of fetal loss before 8 weeks of gestation in order to identify the causes of reproductive losses. The analysis was carried out on 26 women who received treatment with folate group drugs, who made up group 1 and 28 women without pregravidar preparation, who made up group 2.

Keywords: yolk sac, implantation, morphometry, fetal loss.

Preserving reproductive health, ensuring the physiological course of pregnancy and childbirth, and the birth of a healthy, full-fledged child are among the primary tasks of obstetrics throughout the world and are one of the highest priority areas of healthcare in the Republic of Uzbekistan [3,4,10,13].

Among the problems of modern obstetrics, fetal loss, especially in the early stages, occupies one of the leading places in modern healthcare. Despite the well-known successes achieved in embryology, the frequency of losses in early gestation does not have a significant downward trend and, according to various authors, amounts to 5-12% [5,6,7,9].

Every year, about 10% of birth losses in the world occur at the preclinical moment of pregnancy diagnosis [1,8,12,14].

According to modern concepts, up to 80% of early reproductive losses of unknown etiology are caused by immunological disorders, which are usually divided into alloimmune and autoimmune [2,11,15]. In recent years, the greatest attention of researchers has been drawn to the autoimmune aspects of reproductive losses. One of the representatives of which is antiphospholipid syndrome.

Purpose of the study: analysis of the morphological picture of early post-abortion endometrium in women with fetal loss before 8 weeks of pregnancy and homocysteinemia, depending on preconception preparation.

Material and research methods

For a more in-depth study of the pathogenetic mechanisms of fetal loss in hyperhomocysteinemia, data on the results of a morphological study of the early post-abortion endometrium of women in the early stages of fetal loss, up to 8 weeks of gestation, were prospectively examined. The analysis included 26 women who received treatment with drugs of the folate group and group B, who made up group 1, and 28 women who did not undergo preconception therapy, who made up group 2.

In all women, along with a general clinical examination, line scrapings of the endometrium were performed immediately after spontaneous miscarriage to conduct morphometric and morphological studies.

The study was approved by the ethics committee of the ASMI for maternal and child health on the ethics of research on humans. Specimens were obtained under ultrasound guidance and were available in 30 cases ranging in gestational age from 5 to 8 weeks (mean age 7 weeks). Gestational age was assessed by fetal crown length. Immediately after removal, the tissue was fixed by immersion for 2 hours in a 4% formaldehyde solution to obtain blocks for electron microscopy.

Written consent was obtained from all patients and they were informed about the purposes of the study. This study was approved by the Maternal and Child Health Committee of the Andijan State Medical Institute.

Results of our own research

A study of the obstetric history of these groups revealed that the main contingent of the first group had a history of 5 to 7 pregnancy losses; in the second group the same data were revealed.

The most common complications of pregnancy in the study groups are bloody vaginal discharge (56% and 42.85%), threat of miscarriage (65.38% and 53.57%) and impaired blood flow velocity of the uterus (59.2% and 62.85%). 34%) already in the early stages.

In the earliest available sample, whose menstrual age was estimated at 40–50 days, the pattern showed a superficial layer of endometrium of a highly secretory nature. The uterine glands had the appearance of saw teeth, characteristic of the late secretory phase of the menstrual cycle, and were filled with abundant glandular secretions. They were heterogeneous in nature and included carbohydrate-rich flocculent material interspersed with numerous smooth, round lipid-like droplets. Although there were significant differences between samples, there was a statistically significant negative correlation between the two parameters (r=−0.74, P =0.02).

Association with the intervillous space was observed until a gestational age of at least 8 weeks.

In histological preparations of group 1, the following changes were observed: endometrial fibroblastic stromal cells in the stroma of decidual tissue, in which protein-dystrophic changes (hydropic dystrophy, hyaline-droplet dystrophy), necrobiotic changes, autolysis of some, edema in the stroma, focal and diffuse lymphoid changes and macrophages, hemorrhages, a small number of eosinophils, trophoblasts, chorionic epithelium, venous plethora, hemorrhages, nitibux layer, coagulation necrosis (fibrinoid necrosis) of the chorionic epithelium of anchor varicose veins (Fig. 1).

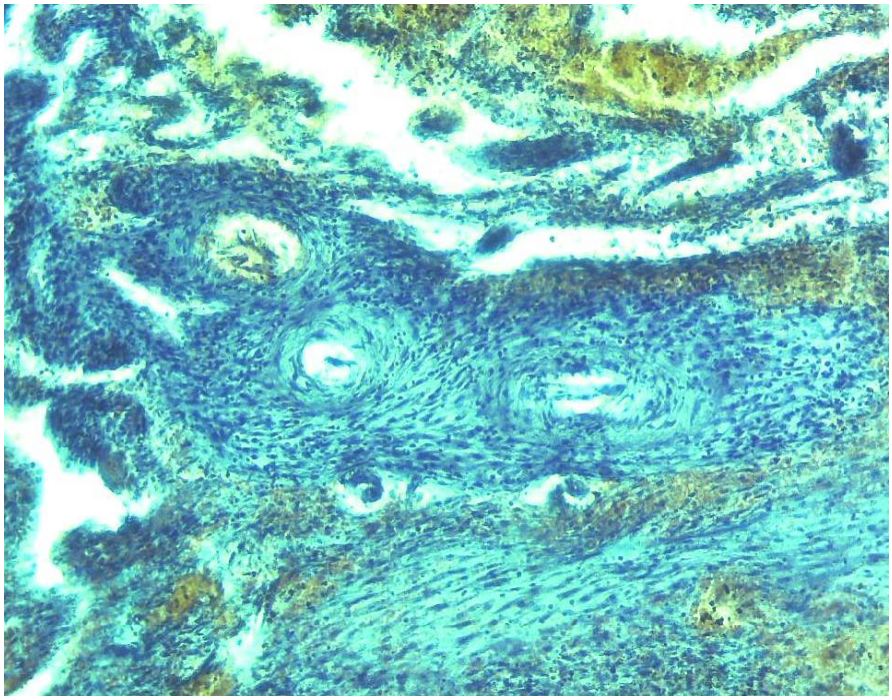

Fig.1. Condition after abortion and curettage, gestational age 6 weeks. On a microslide in the decidual tissue of the stroma, fibroblasts of endometrial stromal cells, in which there are protein-dystrophic changes, edema, infiltration of lymphoid and macrophage cells, venous congestion, hemorrhages. Hematoxylin-eosin staining. Magnification: volume x10, approx x10 (preparation 1-2 x 10(8)).

In group 2 patients, defective endovascular decidual trophoblastic invasion was noted. Necrobiotic changes in decidual tissue, edema, fibrinoid necrosis, venous insufficiency, hemorrhage, lymphoid and macrophage-cellular infiltration.

By 7–8 weeks, endometrial cells in both groups became morphologically more cuboidal in nature with fewer apical projections, although there was significant variation between glandular profiles even within the same sample. The apical cell membrane was often covered with long microvilli, and short filaments of coarse endoplasmic reticulum were present in the cytoplasm.

In each patient, in parallel, on the 20th day after curettage, the sizes of the uterus and endometrium were measured in three projections (length, width and depth) during transvaginal examination. The volume of the endometrium was calculated as an elongated ellipsoid using the formula: (length X width X depth). The experts performing the ultrasound were highly qualified in accordance with the protocol.

Endometrial thickness (P = 0.02), width (P = 0.002), and volume (P = 0.001) were significantly greater in women receiving anticoagulant therapy.

Studies of endometrial regeneration show that the total time for regeneration of the postmenstrual surface of re-epithelialization is approximately 48-72 hours, which occurs on the second and fifth days of the post-abortion period. Since estrogen-dependent changes are not observed until the epithelial surface is restored, it can be assumed that restoration of the endometrial surface does not depend on hormones and results from stimulation of tissue destruction. This process of endometrial surface regeneration has also been observed after spontaneous abortion.

Table I. Comparison of uterine and endometrial indicators

Indicator	1 group	2nd group
Uterus:		
Length(cm)	6.75 ± 0.23	6.24 ± 0.18

Width(cm)	4.28 ± 0.17	4.08 ± 0.14
Thickness(cm)	4.23 ± 0.17	3.97 ± 0.15
Endometrium:		
Length(cm)	3.13 ± 0.17	3.41 ± 0.21
Width(cm)	0.81 ± 0.10	0.64 ± 0.06*
Thickness(cm)	0.84 ± 0.09	0.67 ± 0.06**
Volume (cm^3)	3.85 ± 0.80	1.97 ± 0.40***

* p = 0.002;**P = 0.02; ***P = 0.001.

In contrast to the endometrial surface, in women of group 2 the endometrial stroma was morevulnerable to scraping. Hormone-dependent rapid stromal proliferation was delayed for 2-3 days after curettage and occurred only on the 10th day after curettage. Moreover, the stroma was usually thinner than expected, and the total volume of endometrial tissue remained subnormal throughout the postabortion period.

Adequate endometrial thickness appears to be directly related to uterine vascularity, and women with good endometrial thickness on ultrasound but poor endometrial blood flow tend to have poor reproductive outcome. Uterine perfusion appears to regulate endometrial receptivity, and high uterine resistance to blood flow is associated with recurrent miscarriages. Visualization of the endometrial circulation using three-dimensional Doppler ultrasound shows that the more fetal losses a woman has in history, the higher the risk of failure of another pregnancy, despite the therapy for antiphospholipid syndrome.

Perhaps this fact gives grounds to judge the development of autosensitization in these women, which intensifies with another unsuccessful attempt to carry a pregnancy to term.

Despite the therapy, this group of women experienced another pregnancy loss in the early stages. And analyzing the data obtained, it can be assumed that for an uncomplicated pregnancy in women with a high history of fetal losses, it is apparently advisable to carry out pregestational therapy over a longer period in order to eliminate the occurrence of autosensitization to the therapy and completely restore the reproductive function of the endometrium.

The data obtained may, in the future, after a sufficiently in-depth and complete study, make it possible to more deeply understand the genesis of abortion in sensitized women and optimize a set of measures to prepare for pregnancy and its favorable outcome.

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