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MORPHOLOGICAL CHANGES IN THE REPRODUCTIVE ORGANS OF WOMEN WITH EXPERIMENTAL METABOLIC SYNDROME

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ABSTRACT

In recent years, scientists have been paying increasing attention to metabolic syndrome in women of reproductive age, as it has become one of the most common causes of reproductive diseases. Population studies show that the prevalence of metabolic syndrome in women is 15-20%, while in the structure of reproductive system pathologies, metabolic syndrome accounts for 30-35% and is more frequently detected in patients with recurrent hyperplastic processes. The frequency of endometriosis reaches up to 70%. Numerous studies have demonstrated an increased risk of developing endometrial, cervical, ovarian, and breast cancer in women with metabolic syndrome. It has been established that the prevalence of metabolic syndrome (MS) in women with polycystic ovary syndrome (PCOS) is 43-47%, while the frequency of PCOS in women with MS is 24%. Notably, almost every woman (91%) with PCOS has some components of MS, including dyslipidemia (60%), hypertriglyceridemia (35%), obesity (67%), and arterial hypertension (45%). Most morphological and physiological studies have focused on morphological changes in the heart and pancreas. However, there are few studies dedicated to morphological changes in the reproductive organs of women with metabolic syndrome. Taking this into account, we investigated morphological changes in the uterus and ovaries as the subject of our research. The obtained results revealed that the main morphological substrate consists of changes in the form of destruction and defragmentation in the uterus and ovaries.

Key words: morphology, metabolic syndrome, uterus, ovaries, polycystic ovary syndrome, infertility.

INTRODUCTION

Metabolic syndrome (MS) remains one of the complex problems of modern medical science and practical healthcare, it represents a multifactorial chronic pathological complex of interconnected conditions in the body, metabolic syndrome, hormonal and clinical disorders, and contributes to the development of severe complications, leading to disability, early disability, shortened life expectancy, and a decrease in quality of life. The pathogenesis of metabolic syndrome encompasses several complex mechanisms and includes many unresolved problems. Currently, the frequency of MS in economically developed countries reaches 25-30%, and according to WHO data, the frequency of MS is expected to increase to 50% in the next 20 years. The prevalence of MS among women is 2.4 times higher than among men and reaches 35%. However, there are conflicting data indicating the prevalence of MS among men, and women suffer from this pathology mainly during menopause. Studies conducted in recent years have shown an increase in the frequency of MS among women of reproductive age, young people, and even adolescents. Numerous studies have shown that MS has a high risk of developing cardiovascular diseases (myocardial infarction and stroke), type 2 diabetes, and cancer with a high mortality rate. It has also been proven that MS affects the reproductive system of women with the development of infertility, pregnancy loss syndrome, hyperplastic processes, pregnancy complications (preeclampsia, placental insufficiency, fetal growth retardation syndrome - FGR), which leads to a high incidence of maternal and perinatal diseases.

Aim of research: to study the morphological changes in the female reproductive organs in experimental metabolic syndrome.

Material and methods of research

Mature white laboratory rats weighing 180-200 grams were used as research material. The white rats selected for the experiment were divided into two groups. There were 10 rats in each group. The uterus and ovaries were taken for morphological examination, and the histological sections prepared on a rotary microtome with a thickness of 8-10 microns were stained with hematoxylin, eosin, and Van Gieson. The first control group consisted of 10 rats without clinical signs of somatic and infectious diseases. The rats in the control group were constantly fed free of food and water on a traditional diet. In our second group, we called up an experimental model of metabolic syndrome. After eliminating signs of infectious and somatic diseases, healthy rats were given a diet rich in fat and carbohydrates. The rat diet consists of 60% of laboratory feed, 20% of sheep fat, and 20% of fructose. Instead of drinking water, a 20% fructose solution was administered. The rats were sterilized 30 and 60 days after the experiment. Laboratory white rats in the control and experimental groups were kept in the same vivarium conditions.

Results and discussion

The uterus of rats consists of the following parts - the uterine body, two branches of the uterus, and the cervix. The right and left branches of the uterus are joined to the lower ends at the level of the bladder peak and open into the vagina as separate uterine pores. The branches and body of the uterus include the uterine cavity. The uterine body is a small undivided portion between the uterine horns and the cervix, located in the abdominal cavity on the posterior side of the bladder and in the ventral part of the rectum. To the right and left of the uterine body on the lateral side are paired tubular, relatively long uterine horns. The uterine wall consists of three layers: the mucous membrane, or endometrium, the muscular membrane, or myometrium, and the serous membrane, or perimeter. The uterine mucosa undergoes cyclical changes associated with estrus and ovulation.The mucous membrane of the uterus undergoes destructive and regenerative cyclical changes associated with the menstrual cycle, only between menstrual cycles is it at rest, this period is called the rest period. During rest, the uterine mucosa adheres to the underlying muscular membrane without forming folds, during which the endometrial thickness reaches 1-2 mm and is covered with a single layer of ciliated, cylindrical epithelium. The surface of the uterine body is smooth and there are folds in the cervix. The epithelial cells in the neck area are high (30-60 μm), while in the body area they are relatively low (25-30 μm). Glandular cells of a mucous nature are located between ciliated cells.Such cells are abundant in the cervical part of the uterus. Beneath the epithelium is a thick, private layer of unformed connective tissue with sparse fibers, abundant in cellular elements. The mucous membrane of the uterus contains well-developed uterine glands. The uterine glands are simple tubular ones and are convolutely oriented in the endometrium. The myometrial layer consists of smooth muscle cells, enlarged during pregnancy, sometimes reaching up to 500 μm. The myometrium is divided into 3 layers, the innermost longitudinally oriented layer of muscle fibers, known as the submucosal layer.In the middle layer, muscle fibers are circular, strongly developed and rich in vessels, the outer muscle layer is often made up of smooth muscle bundles lying longitudinally, which consists of the supra-vascular layer. Sparse fibrous unformed connective tissue, rich in elastic fibers, is located between the muscle layers. The perimeter, or serous membrane, surrounds most of the uterus. There is no serous membrane on the anterior and lateral sides of the uterus.

The perimeter is composed of sparse fibrous unformed connective tissue, which is externally covered with mesothelium.The outer surface of the cervical part of the uterus is covered with multilayered squamous epithelium. The cervical canal is made up of mucous cylindrical epithelium. Some ciliated cells are also found between them. The mucous membrane of the cervical canal forms folds, where large cervical glands are present in the specific layer of the mucous membrane. These glands are tubular, branched glands that produce secretions. Under conditions of experimentally induced metabolic syndrome, hypersecretion in the uterine mucosa is observed, a decrease in the number of specific glands located in the specific plate of the submucosal layer, a slight decrease in the number of smooth muscle cells in the myometrium layer, an increase in collagen fibers between them, and a violation of the normal functional state of the uterus. In rats with induced metabolic syndrome, a macroscopic increase in body weight was observed in groups fed a high-calorie diet. The average weight of the experimental rats was 175.25±10.65 g, and on the 30th and 60th days of the experiment, this indicator increased to 215.15±8.45 g. This was accompanied by an increase in body weight and an increase in predominantly fatty inclusions in internal organs and blood vessels. Morphological studies have shown that all internal organs, including the functional epithelium of the endometrial layer in the uterus, are highly active, the amount of mucus increases, the number of closed tubular glands located in the specific submucosal plate decreases, the number of smooth muscle cells in the myometrium decreases slightly, and an increase in collagen fibers is observed. (Fig. 2).

The ovary of rats is covered on the outside with a protein membrane consisting of dense connective tissue, covered with mesothelium. Microvorticles are present on the free surface of the mesothelium. The cortex of the ovary is located beneath the protein membrane, and the cortex is located deeper down. The cortex consists of follicles with varying degrees of maturity located in the connective tissue stroma, an atheric body, periodically - a yellow body, and white bodies. The follicles, depending on the degree of development and structure, are: 1) primordial; 2) primary; 3) secondary; 4) tertiary (pulmonary follicle, Graaf's vesicle, mature follicle). Primordial follicles are the smallest, but most numerous, structures. They consist of a single layer of flat follicular cells and a grade 1 oocyte in the diplotenous period, surrounded by a basal membrane. The primary follicles are characterized by growth of the first-order oocyte, proliferation of follicular cells, and the formation of a glossy membrane. Unlike the primordial follicles, the primary follicles contain cubic or prismatic epithelial cells located in one or two layers on the basement membrane. Microvorticles protrude from the apical surface of follicular epithelial cells and penetrate into the cytoplasm of first-order oocytes. Through these microvorticles, the first-order oocyte receives nutrients that support its growth and development. A second membrane, called a glossy membrane, forms around the 1st-order oocyte. This membrane consists of glycosaminoglycans, mucoproteins, and proteins, which are formed by the functional activity of both oocyte and follicular cells. In follicular cells, organelles associated with the synthesis process, producing products necessary for the growth and development of the oocyte, are well-developed. The size of the follicle increases due to the growth of the oocyte, the enlargement of follicular epithelial cells, and their division. As a result, the connective tissue surrounding the follicle becomes denser, and its connective tissue membrane begins to form. Thus, the primary follicle has the following structure: a primary oocyte in the center, surrounded by a zona pellucida, and cuboidal or prismatic follicular cells arranged in one or two layers on the basal membrane. Growing primary follicles may be involved in polycystic ovary syndrome, which is characterized by enlargement of the ovary with multiple cyst formation and lack of ovulation. Secondary follicles are characterized by cessation of growth of the first-order oocyte. Follicular cells are located around this oocyte, forming a granular layer of several layers. Follicular cells produce follicular fluid containing the female sex hormone estrogen. The fluid accumulates to form the follicular cavity. As the follicle cavity is filled with fluid, its size increases.

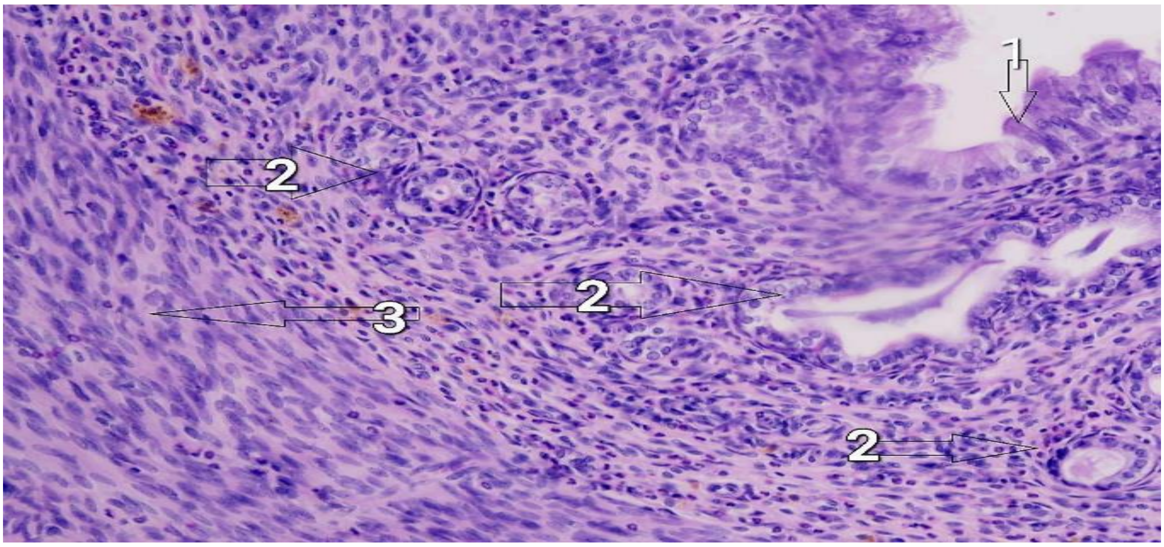

Figure 1. Histological view of the rat uterus in the 30-day control group. Cylindrical mucus-secreting cells in the uterine endometrium (1), fibrocytes and a collagen-rich portion in the submucosal lamina propria layer and closed tubular glands (2), smooth muscle cells visible in the myometrium layer (3). Staining: hematoxylin-eosin. X: 10x40

Under conditions of experimentally induced metabolic syndrome, the cortex of the ovary is unevenly thinned, covered with a single layer of cubic-cylindrical epithelium, with fragments of stromal wounds, white and yellow body cysts. The medullary layer has fibrous stroma and hyaline walls, consisting of vessels of varying sizes. The ovaries exhibit diffuse cell distribution. Mature egg cells are visible in some places (Fig. 5). In rats with metabolic syndrome, a macroscopic increase in body weight was observed in groups fed a high-calorie diet.

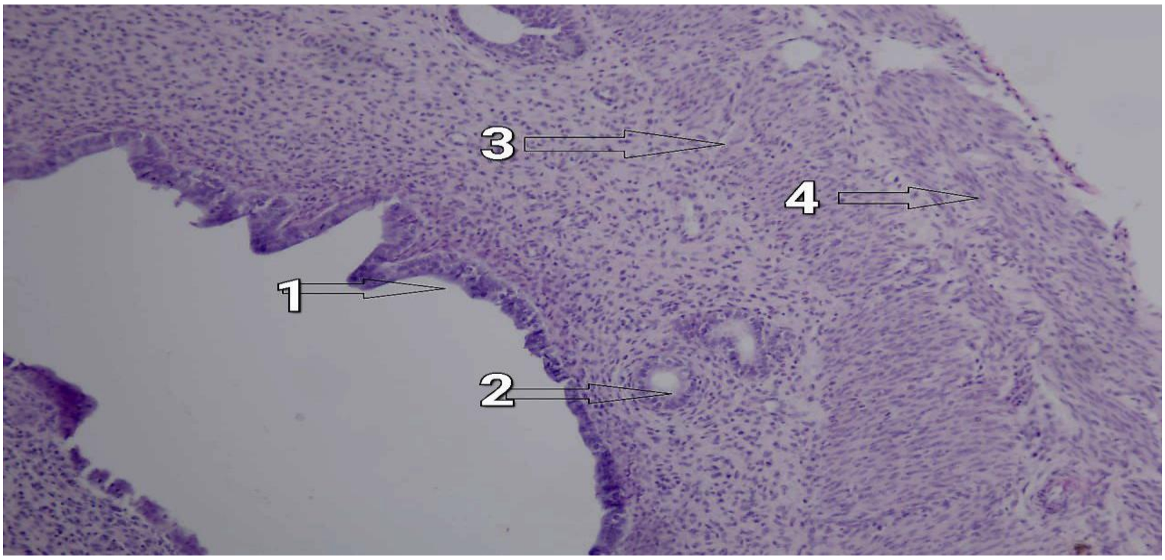

Figure 2. Histological examination of the uterus of rats in the 60-day experimental group appearance. The cells of the endometrial layer are edematous, hypersecretory, and the nuclei are hyperchromatic (1). Staining: hematoxylin-eosin. X: 10x40

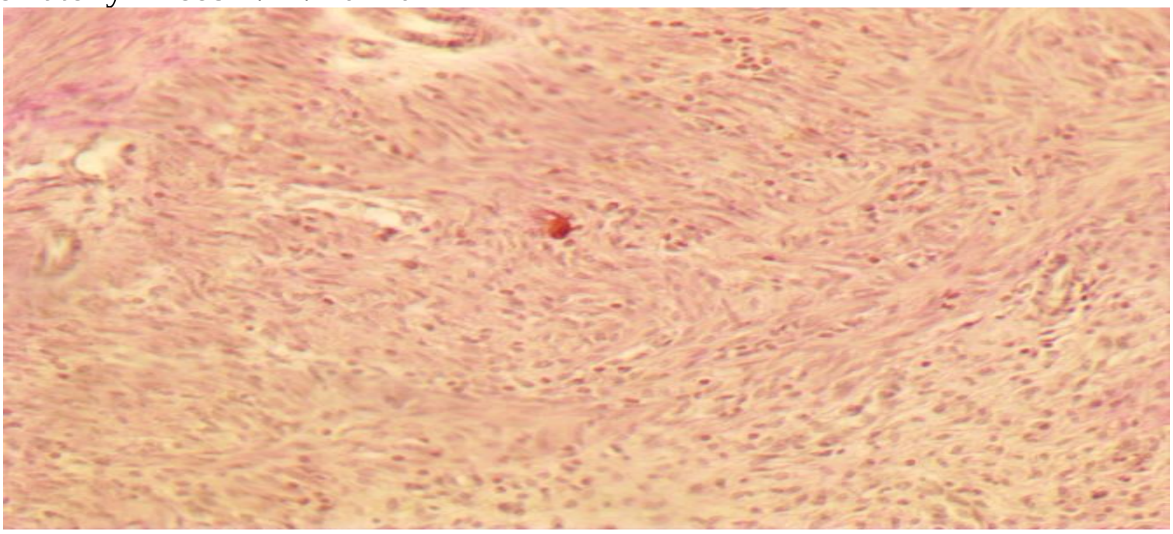

Figure 3. Histological picture of the rat uterus in the 60-day experimental group. Sparse fibrous unformed connective tissue fibers are scattered. Coloring: Van Gieson. X:10x20

In our study, when the uterus was stained with hematoxylin and eosin, the cells of the endometrial layer were slightly edematous, hypersecretory, nuclei were hyperchromatic, the number of simple glands in the layer of sparse fibrous connective tissue of the endometrial propria decreased, blood circulation in the blood vessels was disrupted in the layer of the propria plate, and collagen fibers grew between smooth muscle cells in the layer of the myometrium.

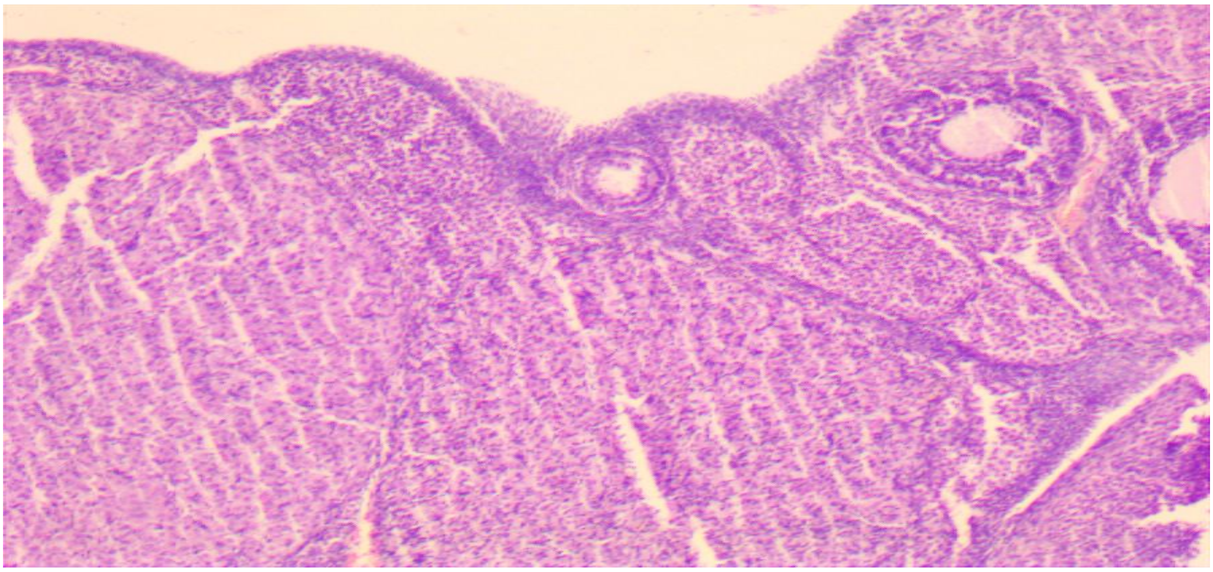

Figure 4. Histological picture of the ovaries of rats in the control group on day 30. The rat's ovary contains an abundant stroma and dense ovary cortex with multiple follicles. A developing primary follicle with prominent granulosa cells is visible near the center, with white bodies of light pink color on the upper right. Staining: hematoxylin-eosin. X: 10x10

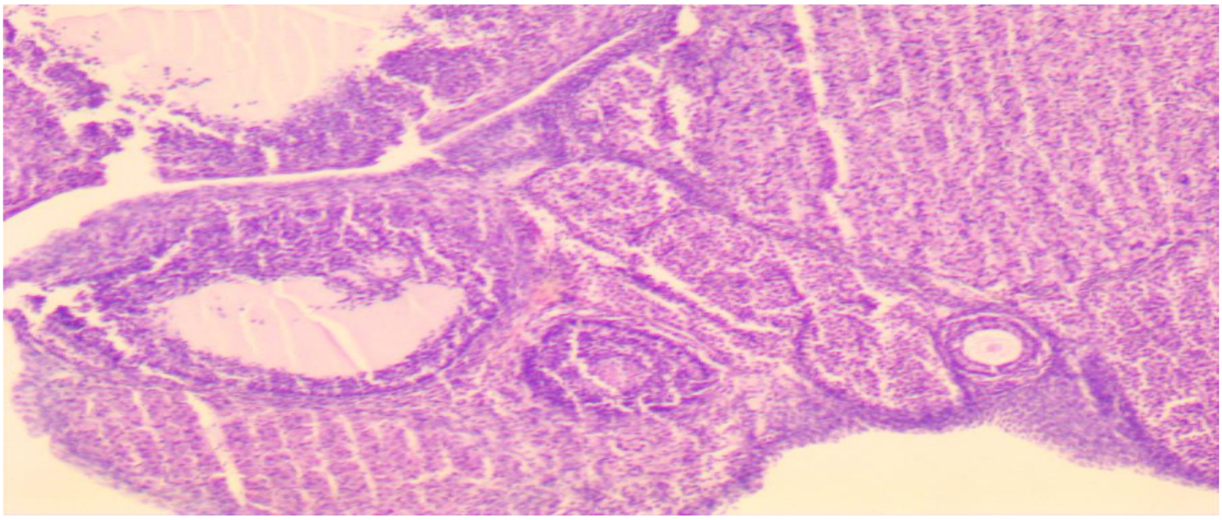

Figure 5. Histological picture of the ovaries of rats in the 30-day experimental group. The cortex of the ovary is unevenly thinned, covered with a single layer of cubic-cylindrical epithelium, with fragments of stromal wound, white body and yellow body cysts. The medullary layer has fibrous stroma and hyaline walls, consisting of vessels of varying sizes. The ovaries exhibit diffuse cell distribution. Mature egg cells are visible in places. Staining: hematoxylin-eosin. X: 10x10.

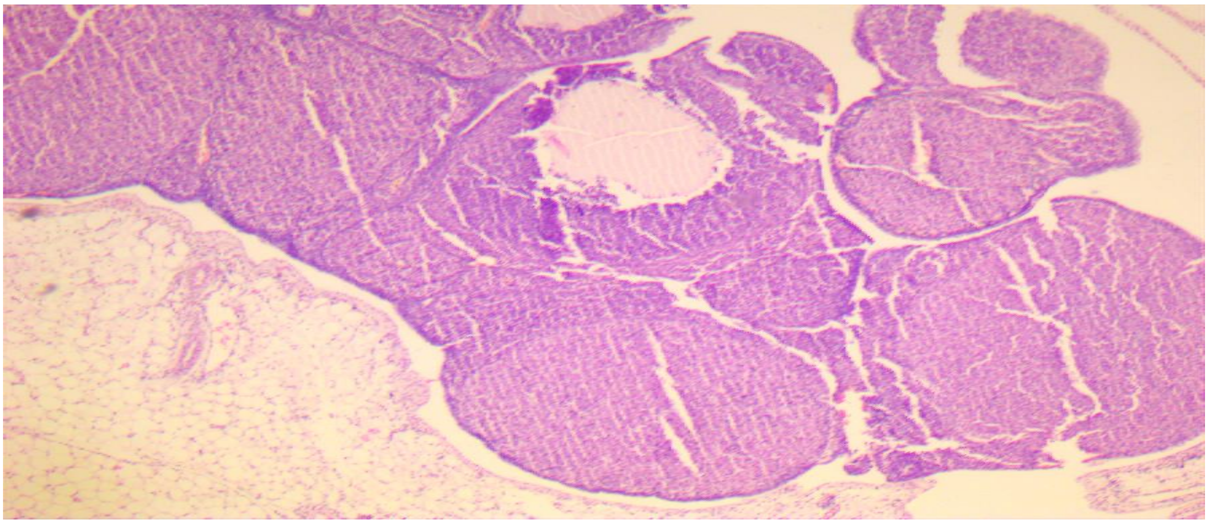

Figure 6. Histological picture of the rat ovaries in the 60-day experimental group.The cortex of the ovary is unevenly thinned, covered with a single layer of cubic-cylindrical epithelium, with fragments of stromal wound, white body and yellow body cysts. The medullary layer has fibrous stroma and hyaline walls, consisting of vessels of varying sizes. The ovaries exhibit diffuse cell distribution. Mature egg cells are visible in places. Staining: hematoxylin-eosin. X: 10x10.

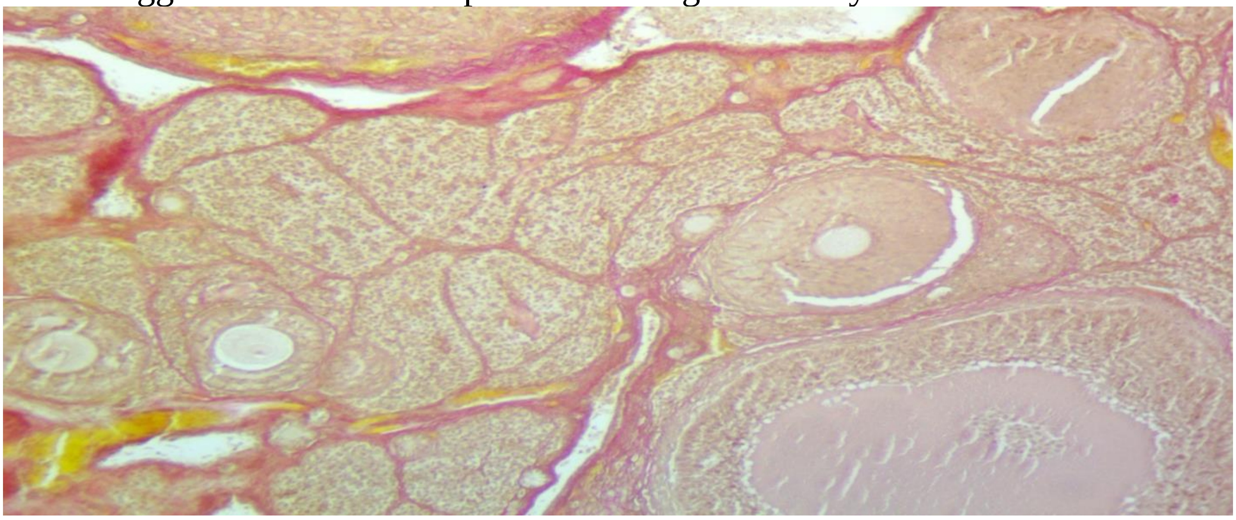

Figure 7. Histological picture of the ovaries of rats in the 30-day experimental group. In the ovary, fibrous connective tissue is encrusted into the ovary parenchyma, the yellow-brown shaded areas are made up of mature follicles of the ovary parenchyma and involuted yellow bodies and white bodies. Fine collagen fibers have grown between the follicles and are slightly thicker than normal. Coloring: Van Gieson. X: 10x10.

Our research shows that when the ovary is stained with Van Gieson, fibrous connective tissue penetrates the ovary parenchyma, while the areas stained with yellow-brown are made up of mature follicles of the ovary parenchyma and involuted yellow bodies and white bodies. It was observed that fine collagen fibers grew between the follicles and were slightly thicker than normal.

CONCLUSION

In rats with metabolic syndrome, the cells of the endometrial layer of the uterus were slightly edematous, hypersecretory, and nuclei were hyperchromatic. In the endometrial plate, we observed impaired blood circulation in the vessels and a decrease in the number of the endometrial glands, which leads to a decrease in the amount of fluid produced by the uterus, resulting in a slowdown in the preparation stage for pregnancy. It was observed that unformed connective tissue with smooth fibers grew into the layer of the myometrium and divided them into fragments, as a result of multiple growth, there was a decrease in muscle elements in the uterine myometrium and an increase in collagen fibers between smooth muscle cells. In experimental metabolic syndrome, the following changes were observed in the ovaries of female rats at 30, 60 days of age: the cortex is unevenly thinned, covered with a single layer of cubic-cylindrical epithelium, with stromal lesions in places, white and yellow body cyst residues. The medullary layer has fibrous stroma and hyaline walls, consisting of vessels of varying sizes. The ovaries show a diffuse distribution of cells. Mature egg cells are visible in some places. It has been established that the fibrous connective tissue penetrates the parenchyma of the ovaries, the areas stained yellowish-brown consist of mature follicles of the ovarian parenchyma and involuted yellow bodies and white bodies. It was observed that fine collagen fibers grew between the follicles and were slightly thicker than normal.

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