Morphological and morphometric characteristics of lymphoid structures in the walls of fallopian tubes in postnatal ontogenesis

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SUMMARY: Morphological and morphometric characteristics of lymphoid structures in the walls of fallopian tubes in postnatal ontogenesis.

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The urgency of the investigated issue is caused by the problem of female infertility, in which the leading cause is the tubal peritoneal factor (the frequency of which does not tend to decrease), as well as inflammatory diseases of the uterine appendages, which lead to the formation of peritubal adhesions and occlusions of the fallopian tubes. Therefore, at present the fallopian tube is considered as one of the important structures in the female reproductive system. The article is aimed at studying the issues of lymphoid structures anatomy in the walls of the fallopian tubes in postnatal ontogenesis.

One of the approaches to investigating this problem is the immunohistological method which makes it possible to reveal the state of the fallopian tubes in women at different phases of the menstrual cycle. For the study, 2000 pairs of fallopian tubes obtained from the corpses of women who died from accidental causes and did not have pathology at the level of the reproductive and immune systems were used. The histological examination of the endometrium was performed. The microanatomical sections of the fallopian tubes were divided into three parts: the isthmus, the ampulla and the infundibulum. Histological sections were stained with standard methods. Variation-statistical processing of the results was carried out by conventional methods.

In the fallopian tubes during the studied periods of postnatal ontogenesis, diffuse lymphoid tissue is constantly present, in which under the influence of hormonal changes there are variously directed changes in the factors of innate immunity. The structure possesses the following characteristic features: it is rich in lymphoid cells the ratio of which changes not only with age but under the influence of external factors.

The hormonal activity causes changes in the lymphoid structures of the mucous membrane of the fallopian tubes, which leads to a decrease in the immune response and causes atrophic changes in the mucous membrane of the female genital organs.

The materials of the article can be useful for the studies developing complex problematics of correlation changes in the fallopian tube in case of its pathology within the genital tract.

KEY WORDS:
Fallopian tube - Diffuse lymphoid tissue - Mucous membrane - Lymphoid structures - Immune structures

Introduction

Recently, interest has increased in the study of morphological changes occurring in the female reproductive system (1). Everywhere in women of childbearing age there is an increase in extragenital pathology, including anemia, in diseases of the reproductive, cardiovascular, endocrine systems and in gestosis, which largely determines the increase in the number of pregnancy and childbirth complications (2). Inflammatory diseases of the reproductive system are characterized by a polymicrobial etiology with predominance of pathogenic microorganisms present in the regular vaginal flora. However, among them sexually transmitted pathogens can also be present (3). The mucous membrane of the fallopian tube is now considered as one of the important structures in the female reproductive system, since it is exposed to numerous antigens.

The incidence peak comes at the age from 17 to 28 years and is clearly associated with sexual activity and the lack of barrier methods of contraception (4). Inflammatory diseases of the pelvic organs are
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among the most widespread diseases in modern gynecology and have a pronounced negative impact on the incidence, quality of life, and female reproductive health (3, 5-8).

Speaking about the health of women of late reproductive age and perimenopause (climacteric period), one should not lose sight of the fact that although women perform professional activities in this difficult period, they still constitute a risk group for extragenital pathology (cardiovascular, digestive, urinary, autoimmune, metabolic disorders, etc.), which is registered in 60% of cases, and in 2/3 of patients this pathology has a chronic character (9). The immune system also undergoes significant changes, the protective properties of all organs and systems are reduced, which contributes to the development of various chronic diseases; therefore, the physiological stress of local humoral immunity is not surprising.

Inflammatory diseases of the pelvic organs are usually the result of an infection ascending from endocervix with the development of endometritis, salpingitis, parametritis, oophoritis, tubo-ovarian abcesses (TOA) and pelviperitonitis. According to numerous studies, in most cases the causative agent is Chlamydia trachomatis (30%) and Neisseria gonorrhoeae (50%), while representatives of the regular genital tract flora (anaerobes, Gardnerella vaginalis, Heamophilus influenzae, Streptococcus agalactiae and Escherichia coli) play an important role in maintaining the inflammatory process (10-13).

Mechanisms of tolerance of the organism are necessary, since the immune system produces a huge number of various antigen-specific receptors, and some of them are specific to the organism's own antigens; thus, tolerance prevents unwanted reactions against own organs and tissues. Overcoming the immune response is also associated with the constant adaptation of the antigen to the action of protective systems and with the possibility of combined attack of the mucosa by various antigens. Bacterial vaginosis, purulent vaginitis, verification of pathogenic microorganisms in the lower genital tract, especially of Chlamydia trachomatis, Neisseria gonorrhoeae and herpes simplex virus, indicates a high risk of contamination of the upper genital tract. According to the research, the absence of leukocytosis in the vaginal discharge testifies to the absence of inflammatory diseases of the pelvic organs with negative predictive value (NPV) up to 95%, while the presence of leukocytosis is unspecific – the positive predictive value is only 17% (14). From this point of view, the organization of the peripheral part of the immune system is of particular interest, since it is subordinated to its functional purpose of recognition and removal of alien agents from the organism (15).

Lymphoid tissue of the mucous membrane of the fallopian tube, like other hollow tubular organs, refers to peripheral tissue (16). As an important structure in the human reproductive process, this membrane is exposed to numerous antigens. These include inflammatory diseases of the pelvic organs, fallopian tubes surgeries, in vitro fertilization, endometriosis, endocrine disorders, intrauterine contraceptives and sexual infantilism (17, 18); sexually transmitted infections have an especially aggressive influence on it (18-20).

At the same time, the inflammatory pathology of the fallopian tubes is one of the most common causes of ectopic pregnancy. Different types of urogenital tract infections of reduces the likelihood of a favorable fertile outcome, since it causes deep, sometimes irreversible, dystrophic changes of the inflammatory character in the endosalpinx. Acute salpingitis in ectopic pregnancy was observed by many researchers; in the available literature, there are also indications of the leading role of chronic salpingitis in the onset of ectopic pregnancy. It is necessary to note a feasible threat to the health of future generations – these are sexually transmitted infections, the frequency of which is especially increased among adolescents (21). This is relevant not only from the point of view of the biological environment, but also from the position of participation in society, as well as in the conditions of developing human relationships influenced by the social factors. Urologists often have to deal with the fact that women have urinary tract and kidney diseases combined with diseases of the genitals, and usually it turns out that the urological disease was preceded by a gynecological disease (17, 19).

The mucous membrane of the female and male genital tract is the pathway for sexual infections of viral, bacterial and fungal origin. The incidence of HIV infection also does not tend to decrease; moreover, according to the world literature, 70-80% of HIV infections occurs through heterosexual contacts, and more than half of the cases are women. Since sexual infections not only affect the health but also can cause infertility, miscarriage, intrauterine fetal death and severe neonatal diseases, direct and indirect economic losses connected to them are huge and significantly increase annually (22).
The main links of the anti-infective protection of the reproductive system are the immune cells and the biologically active substances produced by them, the epithelium of the mucous membrane of the genital tract and the regular vaginal flora. It is known that the state of the immune system depends on endo- and exogenous effects, the most important of which are endocrine.

The mechanisms of anti-infection protection of the genital organs and the influence of exogenous and endogenous factors on it have been studied much less than the immune system of the intestines, oral cavity and bronchopulmonary system, in spite of its critical importance for human reproduction as a species (23).

The first line of protection of the mucous membrane from pathogens is the innate, or the so-called non-specific immunity, which is studied to a lesser extent than the acquired one. It is the first line of defense against infections and includes the epithelial barrier, the cytokines, complement activation and phagocytic response (24).

In this connection, the understanding of the immunomorphological processes occurring in the walls of the fallopian tube acquires a certain importance. By now, the structure of this organ in various periods of ontogeny was studied in some detail, yet the information on its immunomorphology is still fragmentary and contradictory. All of the above causes the relevance of the study of lymphoid structures in the walls of the fallopian tubes.

The aim of the present research is a comprehensive study of the lymphoid structures anatomy in the walls of the fallopian tubes in postnatal ontogenesis.

Methods

For the study, 2000 pairs of fallopian tubes obtained from the corpses of women who died from accidental causes and did not have pathology at the level of the reproductive and immune systems were used. The data were obtained in the study of the mucous membrane of the fallopian tubes of women in the climacteric period, which is confirmed by the control of the histological examination of the endometrium. The microanatomical sections from three parts of the fallopian tubes were studied: the isthmus, the ampulla and the infundibulum. Histological sections were stained with hematoxylin and eosin and picofuchsin according to van Gieson. Variational-statistical processing of the obtained results was carried out by conventional methods (25, 26). The received digital material was processed by variational statistics methods on a PC with the MS Office software package. The reliability of the difference in frequencies was determined using the chi-squared test, (for two to two tables in the Fisher Exact test). The reliability of the mean difference in groups was checked by the variance analysis (26). The applicability of this method was verified by analyzing the size of the groups and the nature of the distribution, including the calculation of the eccentricity coefficient. In doubtful cases, the comparison was duplicated using similar methods of nonparametric statistics.

Results and discussion

Lymphoid formations in the walls of the fallopian tubes are represented by diffuse lymphoid tissue. Lymphoid nodules were not detected.

The cellular composition of diffuse lymphoid tissue of the fallopian tubes is very similar throughout the postnatal ontogenesis and is represented by reticular cells, fibroblasts, small and medium lymphocytes, plasma cells of varying degrees of maturity, destructively altered cells, granulocyte cells (eosinophils, neutrophils), single macrophages and mast cells.

In the diffuse lymphoid tissue of the fallopian tubes, small and medium lymphocytes are located in the mucosa and submucosa, are present as single cell elements, and lie in pairs, groups, or in the form of short chains consisting of 3-5 lymphocytes. In the proliferative phase of the menstrual cycle in both fallopian tubes the number of medium lymphocytes in adolescence did not exceed 5.1%; their content was uneven throughout the entire length of the fallopian tube, and the main quantity occurred on the own plate of the mucous membrane of the uterus. In the older age groups, their number increases 1.9 times in the second period of adulthood, while in the climacteric period their relative content does not exceed 2.9% of all the cells. At the same time, in the secretory phase of the menstrual cycle in the mucous membrane of both fallopian tubes the number of...
medium lymphocytes gradually increases towards the first period of adulthood, reaching 8.7%, followed by a 1.3 decrease in the right fallopian tube and a 1.4 increase in the left one in the second period of adulthood. The number of small lymphocytes in the proliferative phase of the menstrual cycle in adolescence is 15.2%, with clusters of lymphocytes predominating in the lamina propria of the mucosa, and an increase in their number towards the infundibulum of the right fallopian tube. Concerning the age aspect, the dynamics of these forms of lymphocytes changed towards an increase to the 1st period of adulthood, reaching the maximum in the ampulla (21.7%). It should be noted that the increase in lymphocytes comes from the lamina propria to its secondary folds, along the entire length of the fallopian tube. In the secretory phase of the menstrual cycle, the maximum content of these cells in adolescence is 24.4% and in the second period of adulthood 20% (in the secondary folds of the mucosa of the ampulla). The exception is the adolescence and the first period of adulthood, where the number of these cells is stable and does not exceed 15.2-17.9%. In the menopausal period, the content of small lymphocytes predominates in the right fallopian tube by 1.4 times, in comparison with the left fallopian tube.

Thus, with the development in reproductive life, the content of lymphocytes varies unevenly in the diffuse lymphoid tissue of the fallopian tubes – the periods of their accumulation in young age groups (adolescence) are recorded, which is associated with the processes of enhanced human growth and maximum development of lymphoid formations (18, 27-29). The increase in the number of lymphocytes observed in the older age groups is associated, apparently, with emerging somatic problems, affecting the immunological state of the entire genital apparatus (15, 28). At the same time, the uneven distribution of lymphocytes in different phases of the menstrual cycle is explained by the peculiarities of dyshomoronal processes – the combined effect of hormonal factors (progesterone, estrogens) and readiness for increased antigenic stimulation of the fallopian tube tissues.

It should be noted that innate immunity is activated by molecules of microorganisms (zymosan, lipopolysaccharides, flagellin, etc.) binding to Toll-like receptors which are found on phagocytes and epithelial cells. This binding leads to the secretion of antimicrobial peptides (defensins) and the release of chemokines that attract phagocytes to the affected area, trigger the cytokine cascade, activate natural killer (NK) cells and lymphocytes (30). Epithelial cells of the female reproductive system express 10 types of Toll-like receptors (TLR), each of which binds only to specific ligands (14, 31, 32). In each department of the female genital organs, Toll-like receptors are not expressed uniformly, so in the endometrium and fallopian tubes TLR 2 and 4 expression is much greater than in the cervix (14). Recent studies show that the expression of Toll-like receptors also depends on the phase of the menstrual cycle, but the research data are contradictory. Thus, Hirata et al. (2007) suggest that mRNA expression of TLR 2-4 and TLR 9 is higher in the premenstrual period (33), while Aflatoonian et al. (2007) reveal peak mRNA expression of TLR 2-6, TLR 9 and TLR 10 in the secretory phase of the cycle (31). According to a number of researchers, in vitro experiments reveal that Toll-like receptors actively function in all the departments of the female reproductive system. Thus, a reaction was obtained in the form of enhanced cytokines production in response to stimulating the cultures of epithelial cells of the endometrium, cervix and fallopian tubes with polycytidylic acid (poly I: C), which is a ligand of TLR-3 (34). It was also established that oviduct fibroblasts and endometrial epithelial and stromal cells are capable of increasing the release of inflammatory mediators in response to a lipopolysaccharide that is a ligand of TLR-2 (35). These in vitro data suggest that Toll-like receptors in the reproductive tract cells of a woman respond to the pathogen in vivo and induce an immune response by lymphocytes.

It should also be noted that with age, the number of destructively altered cells in diffuse lymphoid tissue also increases, so in the menopausal period in the mucosa it varied from 18.6 to 31.9% in different parts of the fallopian tube. When comparing the distribution of destructively altered cells between both tubes, the largest number is in the own plate of the ampullary mucosa of the left tube, reaching 39%, which is 1.3 times greater than in the same structural zone of the right tube. In addition, in the early menopause in the mucous membrane of both fallopian tubes macrophages, mast cells, eosinophils and neutrophils were observed, the number of which reached single values, and slight increase in their number in the ampullary part of the uterine tube (in primary folds) to 1.4% was noted. Very stable content of these cells in the infundibulum was also observed, reaching 0.5% (in the own plate and the sec-
References


19. Kuznetsova MA, Zolotareva MA, Miroshkin DV. General pat-
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