IJIMM, Volume 2, Issue 6, 2024 ISSN: 2995-5319
http://medicaljournals.eu/index.php/IJIMM/issue/view/3

INTERNATIONAL JOURNAL OF INTEGRATIVE AND MODERN MEDICINE

Immuno-Allergological Aspects of Infertility in Men

Saidov Akmal Abdullaevich
Bukhara State Medical Institute

Abstract: According to a new report published today by the World Health Organization (WHO), a very large number of people will experience infertility during their lifetime. Infertility affects approximately 17.5% of the adult population, or approximately one in six people worldwide, highlighting the urgent need to expand access to affordable, high-quality fertility treatments for all those in need. Among infertile men, autoimmune disorders, according to various sources, range from 3 to 36%. The cause of decreased male fertility may be immunological disorders associated with autoimmune reactions against sperm with the formation of antisperm antibodies.

Keywords: infertility, immune system, men, allergies, sperm.

Relevance. According to current concepts, the mechanism of formation of antisperm antibodies is associated with the fact that the tolerance of the immune system to its own antigens is formed during embryonic development, when there are no sperm. In addition, spermatozoa have a chromosome set different from somatic cells. In this regard, the immune system perceives sperm antigens as foreign. And when those appear, they must be completely separated from it. For the testicle, this function is performed by the blood-testis barrier, in other parts of the male reproductive system - by the epithelial lining and local immunosuppressive barrier (Comhaire, 2011). According to the results of one of the large-scale studies, antisperm antibodies are found in 18% of men of reproductive age (O.V. Teodorovich, 2005). The importance of sperm-associated antibodies of the IgG or IgA class in the development of infertility is noted (Yu. Alyaev, M. Gazimiev, 2008). Factors in the development of antisperm antibodies are mainly a violation of the integrity of the epithelial or blood-testis barrier; they can arise as a result of their mechanical, infectious and other damage. Also, antisperm antibodies can arise due to obstruction of the vas deferens, cross-reaction between antigenic determinants of sperm and infections of the reproductive tract, and peculiarities of anti-infective immunity (probably inherited).

According to Western scientists, the main reason for the “leakage” of antigens leading to the formation of antibodies is vasectomy (A. Mahmoud, F.R. Comhaire, 2011). According to V.A. Bozhedomova and A.V. Teodorovich (V.A. Bozhedomov, O.V. Teodorovich, 2005), the most common potential risk factor for the development of immune infertility is infections of the reproductive tract. However, the likelihood of this pathology occurring during infections is significantly lower than with subclinical injuries to the scrotal organs. Such mechanical injuries can be either single significant (for example, a fall on an object, a blow), or habitual unexpressed (wrestling and other combat sports, horse riding, motorcycle sports) (V.A. Bozhedomov, O.V. Teodorovich, 2005).

The disappearance of an infectious pathogen under the influence of antibacterial therapy is mainly accompanied by a decrease in the number of sperm coated with antibodies (V.A. Bozhedomov, O.V. Teodorovich, 2005; A. Mahmoud, F.R. Comhaire, 2011). However, with the initial level of such sperm being more than 58%, the chances of a significant decrease in the activity of antisperm immunity after treatment of the infection (in particular chlamydia) are very low. Varicocele increases the risk of autoimmune reactions and orchitis after injury (V.A. Bozhedomov, O.V. Teodorovich, 2005). In the presence of antibodies, sperm motility decreases, their agglutination occurs, their passage through the cervical canal into the uterus becomes impossible, the acrosomal reaction is disrupted, without which fertilization of the egg is difficult even in vitro (H.M. Behre, E. Nieschlag, D., 2005; Yu. Alyaev , M. Gazimiev, 2008).

As is known, the presence of antisperm antibodies (ASAT) in a man does not respond to conservative therapy (M.L. Check, J.H. Check, D. Katsoff, D. SummersCChase, 2000). Despite the fact that several studies have proven the lack of correlation between AST levels and ICSI outcomes (S.C. Esteves, D.T. Schneider, S. Jr. Verza, 2007; A. Zini et al., 2011), in the case of combined pathospermia, the pathogenesis of disturbances in ejaculate parameters during immunological infertility is associated with oxidative stress (V.A. Bozhedomov et al., 2015). Aseptic inflammatory changes in the genital organs in some cases have an autoimmune origin, in others – dishormonal, in others – vegetoneurotic genesis.

Chemical substances, penetrating into the body, are metabolized and converted into even more aggressive substances - xenobiotics. The immune system has become the subject of close attention and study as a target of xenobiotics relatively recently. It has been proven that widespread contact with a variety of chemical compounds in a significant part of the population serves as a source of stimulation of IgE and leads to an extension of the local tissue reaction to the generalization of the process. The level of IgE in healthy people varies widely – from complete absence to a significant increase. Its concentration increases until puberty, and then gradually decreases. Violation of the main function of the immune system - the ability to protect the internal environment of the body from foreign agents - occurs at the cellular and humoral levels, and then manifests itself in hypersensitivity reactions, insufficient production of antibodies, autoimmune reactions and proliferative diseases of this system. Sensitization occurs as a result of contact with the antigen. A change in the body's reaction upon repeated contact with a certain antigen is a consequence of allergic restructuring - sensitization, which occurs as a result of the formation of specific antibodies in the body. The most important causes of the formation of antibodies against sperm are cryptorchidism, postoperative varicocele, obstructive azoospermia, various inflammations of the testis and epididymis. Allergic reactions are more often regarded as harmful to the body. However, from the point of view of biological expediency, it is right to classify them as adaptation reactions, since, by helping to free the body from foreign substances, they ultimately ensure the preservation of antigen homeostasis.

Modern studies have found that inactivation of ubiquitin protein ligase, localized in male germ cells, leads to blocking spermatogenesis and the development of infertility. Taking this into account, it can be assumed that structural and functional damage to the components of the ubiquitin proteasome system can play a significant role in the pathogenesis of male infertility of various etiologies, and, in particular, when exposed to ionizing radiation (S.V. Bazalitskaya, 2011). The immunohistochemical features of the expression of the Ubiquitin protein in the testicular tissue of patients with severe forms of male infertility - excretory-obstructive and secretory - were studied. Molecular changes in the ubiquitin-proteasome system, characteristic of the secretory form of the male asympathetic cycle and the rate of transcription in interstitial endocrinocytes - Leydig cells, and an increased content of damaged intracellular proteins in Leydig cells and Sertoli cells in these patients were revealed (S.V. Bazalitsk). aya, A.M. Romanenko , 2011). A significant decrease in the level of immunohistochemical expression of the Claudin 11 protein was revealed in the secretory form of male infertility and the "Sertoli cell only" syndrome, compared with excretory-obstructive infertility. The results indicate significant violations of the GTB, which are the basis for the development of an additional immune component and the intensification of pathological changes in patients with the secretory form of male infertility (S.V. Bazalitskaya, 2012). The possibilities for studying the causes of infertility in men have expanded significantly thanks to the deciphering of the human genome, sequencing of the Y chromosome and the introduction of modern molecular technologies into medical practice. The authors examined 80 men with idiopathic infertility. Eighteen patients with a concentration of sperm in the ejaculate underwent a genetic blood test for the presence of deletions in the AZF locus of the Y chromosome. Isolation and purification of DNA from venous whole blood was carried out using a standard nucleic acid precipitation method. To analyze variations in deletion regions of the AZF gene, specific DNA amplification was carried out in vitro.

Pretesticular causes of infertility: – pathology of the hypothalamus region; – isolated deficiency of gonadotropins (Kalman syndrome); – isolated deficiency of luteinizing hormone ("fertile eunuch"); –

isolated FSH deficiency; – congenital hypogonadotropic syndrome; – pathology of the pituitary gland; – pituitary insufficiency (tumors, infiltrative processes, operations, radiation); – hyperprolactinemia; – hemochromatosis; – the influence of exogenous hormones (excess estrogens and androgens, excess glucocorticoids, hyper and hypothyroidism) Kallmann syndrome, manifested by an isolated deficiency of gonadotropins (LH and FSH), occurs both in the form of sporadic mutations and in familial form. And, although the incidence of the disease is low (1 case per 10,000 men), it is the second cause of hypogonadism after Klinefelter syndrome.

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