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Purulent-Destructive Diseases of the Scrotal Organs and Modern Possibilities of Pathogenetic Therapy

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Abstract: Acute epididymitis – one of the most common urological disease in men at any age. With a number of serious complications, leading eventually to the development of infertility, epididymitis is a fairly serious health and socio-economic problem. Etiological agents in young people are agents of urogenital infections, and in older adults - a Gram-negative intestinal flora. In the pathogenesis of dominant intracanalicular pathway. We also show the negative impact of acute epididymitis change tissue hemodynamics, immunoreactivity of the body and on the reproductive function in men, explained the mechanism of autoimmune infertility. In addition, modern approaches to the treatment of acute epididymitis, which is the basis of antibiotic therapy with the possibilities of physical therapy action and local treatment. In the case of complicated forms of epididymitis exhibited indications for surgical treatment.

Keywords: acute epididymitis, acute orchiepididymitis, pathogenesis, diagnostics, treatment.

Acute epididymitis is an infectious and inflammatory disease of the epididymis lasting less than 6 weeks. In some cases, the testicle is involved in the inflammatory process along with the appendage, and then we are talking about epididymoorchitis.

In the structure of emergency urological morbidity, the proportion of acute epididymitis is 4 - 10% [1, 3].

According to the results of studies conducted in the USA, acute epididymitis is the fifth most common urological disease for men aged 18 to 50 years. At the same time, more than 800,000 men suffering from acute epididymitis (2022) apply to medical institutions in the United States every year [2].

Most authors agree that the most common (up to 80% of cases) acute epididymitis occurs in men aged 20 to 40 years. The average age of patients with acute epididymitis, according to a study conducted in London, is 28 years.

Kaver SR et al. (2000), based on the analysis of 121 case histories, provides other data. The distribution of patients with acute epididymitis by age in their study was bimodal, and the peaks of morbidity occurred at the age from 16 to 30 years and from 51 to 70 years [1].

In persons who have not reached puberty, acute epididymitis is much less common. According to a study carried out in Israel, the annual incidence of epididymitis in boys from 2 to 13 years is 1.2 per 1000 people. At the same time, most often it occurs as a reaction to systemic inflammatory diseases and has a benign course.

The disease is predominantly unilateral, a bilateral process is observed in 10% of patients. The spread of the inflammatory process to the testicle with the development of acute epididymoorchitis is observed, according to various authors, in 10-60% of cases [3].

Surgical treatment associated, as a rule, with the development of purulent-destructive forms of the disease (most often - appendage abscess) is performed by 10 to 20% of patients with acute epididymitis.

In 20% of patients, as a result of acute inflammation, a chronic inflammatory process is formed in the appendage of the testicle, which in turn causes sclerotic, dystrophic changes in it, impaired patency of the vas deferens, leading to the development of obstructive infertility. The frequency of infertility after orchoepididymitis is 20-35% with unilateral lesion and 80-85% with bilateral process [2, 3-4].

ETIOLOGY

Historically, most cases of acute epididymitis in men of reproductive age were considered idiopathic, believing that the cause was reflux of sterile urine into the vas deferens during forced urine extrusion through the closed external urethral sphincter. Graves RS and Engel WJ (1950) even modeled this condition on dogs, confirming this theory. However, it was subsequently shown that such forced urination occurs in less than 10% of patients. In addition, it was found that with reflux of sterile urine, neither pyuria nor urethritis can develop, however, these symptoms are present in most young patients with epididymitis [4].

The results of recent studies have shown that in young men under the age of 35, epididymitis and orchoepididymitis are most often caused by sexually transmitted infections, such as Chlamydia trachomatis or Neisseria gonorrhoeae, while in elderly patients epididymitis is usually caused by gram-negative intestinal flora.

In men of the older age group, microorganisms found in urine become frequent pathogens of epididymitis. The reason for this is obstructive diseases of the lower urinary tract - urethral strictures, obstruction of the bladder neck, benign prostatic hyperplasia. In these diseases, incomplete emptying of the bladder, increased pressure in the posterior urethra during urination contribute to reflux of infected urine into the vas deferens and the development of epididymitis [5]. The most common etiological factor in this age group is Escherichia coli, it is detected in 30%-50% of patients with acute epididymitis, there are other uropathogens - Enterococcus faecalis, Proteus mirabilis, Pseudomonas aeruginosa. In the study of V. N. Mironov (2003), as a result of the use of bacterioscopic, bacteriological research methods and PCR diagnostics, the etiological agent of acute epididymitis was detected in 75% of the examined patients. At the same time, sexually transmitted infectious agents (Chlamydia trachomatis, Mycoplasma genitalium, etc.) were of primary importance in the etiology of acute epididymitis in men younger than 45 years, conditionally pathogenic microflora was detected in 25% of cases, and a combination of the two above-mentioned types of microorganisms was observed in the vast majority of patients. In patients of the older age group, both saprophytic microflora in the form of staphylococci (Staphylococcus epidermalis, Staphylococcus saprophyticus) and gram-negative conditionally pathogenic microflora are detected [6].

Similar data were obtained in the study of Razina S. E. (2010) - sexually transmitted infections (N. gonorrhoeae, C.trachomatis, T.vaginalis), were the etiological factor of acute epididymitis in 43.2% of cases (mainly in the age group under 35 years). In patients over 35 years of age, the etiological structure of acute epididymitis was different - E.coli (34.9%), Proteus mirabilis and Staphylococcus spp. (27.9% each).

In acute epididymitis in patients under the age of 40, U. urealyticum is detected in 15% of cases, however, the clinical significance of this microorganism currently remains uncertain, since U. urealyticum is detected in a significant number of healthy individuals [7].

In the last decade, the role of M.genitalium in the development of inflammatory urogenital diseases of both sexes has been actively studied, but convincing evidence has been obtained only about the

involvement of the microorganism in non-gonococcal urethritis in men. Infectious epididymitis can also develop as a result of various medical manipulations and surgical interventions on the urinary tract, such as bladder catheterization, permanent transurethral drainage, cystoscopy, prostate surgery [7].

According to domestic studies, acute epididymitis complicates the course of 2-8% of transurethral surgical interventions, while if cystostomy drainage takes place or bladder catheterization was performed before the operation, the complication rate increases to 20% [8].

PATHOGENESIS

4 possible ways of getting infectious agents into the appendage of the testicle are described:

1) hematogenic (the development of epididymitis is preceded by angina, sinusitis, furunculosis, sepsis and other infectious conditions);
2) lymphogenic - along the lymphogenic path:
3) ascending path (canalicular) - along the vas deferens:
4) secretory - epididymitis is preceded by orchitis (this pathway is typical for the viral nature of the disease). Most authors point out that the canalicular pathway is the most frequent [6].

The predominance of the canalicular pathway of infection is also evidenced by clinical observations: in epididymoorchitis, the appendage of the testicle is always affected first of all, and destructive changes occur more often in the tail of the appendage than in the head [10].

Approximately 10% of cases of inflammation of the epididymis appendage relate to post-traumatic epididymitis, which develops against the background of trauma to the scrotum organs, more often complicated by testicular rupture, testicular parenchyma infarction or intratesticular hematoma, as well as after surgical interventions on the testicle and appendage [9].

Morphological changes in the initial stage of acute epididymitis are represented by infiltration of the interstitial tissue of the appendage, swelling and thickening of its shell, accumulation of serous exudate in the lumen of the appendage [10].

A frequent and natural complication of acute epididymitis is the development of orchitis, which is caused both by the direct spread of the inflammatory process towards the testicle perivasally and interstitially, and indirectly, due to mechanical factors - circulatory disorders, lymph circulation, testicular compression, stasis and hypertension in the ducts and seminal tubules. At the same time, similar changes occur in the testicle - infiltration of the stroma by leukocytes, accumulation of exudate in the tubules, thickening of the protein membrane [10, 11-13]

With the progression of the disease, the process turns into a purulent form with the formation of microabcesses, an abscess of the epididymis, or an intratesticular abscess, which complicate the course of acute epididymitis in 5% of patients. Limited abscesses can end in self-healing with an outcome of scarring or calcification, but more often lead to focal or diffuse sclerosis of the testicle or appendage. The inflammatory process in the appendage may end with obliteration of the duct of the appendage, which in a bilateral process becomes the cause of infertility [13].

Transient immune disorders play a certain role in the pathogenesis of acute epididymitis. The literature presents various data on the nature of immune changes in patients with acute epididymitis, which are often contradictory.

In the study of Boris Yu. B. et al. (1996) the immune status of patients with acute epididymitis was assessed both on the severity of the inflammatory process (1st day after the onset of the disease) and when the inflammatory process subsided against the background of successful therapy. At the same time, it was found that the "peak" of the acute inflammatory process is characterized by a decrease in the level of T-lymphocytes, with an increased relative number of T-helpers and a reduced level of T-suppressors, as well as a high ratio of CD4+/ CD8+, the number of B-lymphocytes remains unchanged [12]. When the acute inflammatory process subsides, a low content of T-lymphocytes is observed, the number of T-suppressors increases, the level of T-helpers decreases, the CD4+/CD8+

ratio is lower than in the acute period, the number of B cells increases. On the part of humoral immunity and phagocytosis, an increase in the amount of IgG and an increase in phagocytosis indicators were revealed against the background of the subsiding of the acute inflammatory process, which has a beneficial effect on the course [18].

Bratchikov O.I. et al. (2000) in their study point to the important role of autoimmune rearrangement in the pathogenesis of acute epididymitis - sperm agglutinating antibodies belonging to the IgG and IgM class appear in the blood of patients, as well as immunomobilizing antibodies binding the C3 component of the complement [13].

Alchinbayev M.K. et al. (2005) evaluated the possibility of using immunological indicators to predict the course of the inflammatory process. The authors regarded the state of the cellular link of immunity as a transient immunodeficiency, which is characterized by a low level of T-lymphocytes, an almost twofold decrease in the helper subpopulation with a relatively stable CD8+ content. Damage to the hematotesticular barrier complicates the course of acute epididymitis with autoimmune orchitis with a rapid increase in the CD16+, CD56+ subpopulations identified as "natural killers" (NK cells) up to 38.9± 4.1%. Based on this, the authors conclude that the detection of more than 15% CD16+, CD56+ in patients with acute epididymitis indicates the involvement of the testicle in the inflammatory process. During the transition from serous to purulent inflammation, the authors noted the defectiveness of phagocytosis mediated by immunoglobulin and complementary receptors - the expression level to the Fc fragment of IgG reached 86%, and to complement - 60% [13, 15].

The development and progression of acute epididymitis is accompanied by disorders of the organ blood flow, both in the appendage and in the testicle [14].

Aboev Z.A. (2001) during dopplerography of testicular vessels in patients with acute epididymitis revealed an increase in blood flow in the testicular arteries on the affected side by 40-90% compared to the norm. Similar data were obtained in a number of other studies, which made it possible to consider increased blood flow as an important criterion for the diagnosis of acute epididymitis [17].

Brown J.M. et al. (1995) showed that acute epididymoorchitis is characterized by an increase in the peak systolic blood flow rate in the vessels of the testicle and its appendage over 15 cm/sec, which is significantly higher than in the organs of the scrotum on the contralateral side. In this regard, the author recommends as an additional criterion for the presence of acute inflammation of the scrotum organs to use the ratio of the peak systolic blood flow rate on the affected side to a similar indicator of the contralateral side. According to the author, in the case of acute inflammation in the appendage of the testicle, this indicator will be equal to or greater than 1.7 and for the testicle it is equal to or greater than 1.9. At the same time, in this study there were no changes in the resistance index compared with the control group [22].

However, in another study performed by Wilbert D.M. et al. (1993), it is reported that in more than half of cases with epididymoorchitis, the resistance index was below 0.5, while in healthy volunteers this indicator is rarely less than 0.5. However, in the same study, 3 patients with epididymitis had no significant changes in blood flow [16, 18].

Severe epididymitis can lead to testicular tissue ischemia, both due to the involvement of testicular tissue in the inflammatory process, as well as due to compression of testicular blood vessels by the edematous tissue of the appendage [18].

The effect of acute epididymitis on the reproductive function of men

The appendage of the testicle is an important reproductive organ that provides the final functional completeness of sperm necessary for fertilization. The role of the appendage of the testicle in ensuring male fertility is determined, in particular, by such functions as transport, reservoir, secretory and the function of sperm maturation [25].

The frequency of infertility after orchoepididymitis, according to Kuzmin M. D. (2002), is 20-35% with unilateral lesion and 80-85% with bilateral process [24].

In the study of Kalinina S. N. (1991), other data were obtained, according to which the incidence of infertility after epididymitis reaches 72-76.6% [26].

Infertility after acute epididymitis is most often of an excretory obstructive nature associated with obstruction of the duct of the appendage and accounts for 10.5% of all cases of male infertility.

However, the pathogenesis of spermatogenesis disorders in epididymitis has not been sufficiently studied. In some cases, the causes of infertility are identified quite easily, but in about 30 to 50% of cases, the determination of the etiological factor is very difficult or impossible [29, 30].

The presence of pathospermia persisting for a long time after acute epididymitis has been demonstrated in a number of studies.

Shapoval V. I. et al., (1990) studied the parameters of the ejaculate 3 months after the treatment of acute epididymoorchitis, while the average volume of the ejaculate was 3.3 ml., normospermia was observed in 36.3% of patients, oligospermia of the first degree - in 22.8%, third degree - in 13.7% of patients. Aspermia and azoospermia were not observed [19].

According to Ukhal M.I. et al., (1990) on the 12th day from the onset of the disease, in the analysis of the ejaculate of patients treated conservatively and operatively, there is a decrease in the total number of spermatozoa and an increase in the number of pathological forms (up to 60-70%). After 6 months in patients treated conservatively, oligozoospermia and pathozoospermia persisted in 67%, and after a year in 54%. In the group of patients where surgical treatment was used, these indicators remained in 12% and 6%, respectively [28, 29].

Bogomolny N.G. and Buchumensky V.B. (1990), studying the indicators of ejaculate in patients with acute epididymitis, noted the following changes: an increase in the number of pathological forms of spermatozoa (43.5 ± 1.99%) and spermatogenesis cells (21.4± 6.7%), pyospermia (16.8± 1.37 leukocytes in the field of vision). In addition, the authors revealed a decrease in the content of potassium, sodium, magnesium and, especially, calcium and zinc in the ejaculate, which, in their opinion, indicates both energy disorders and inhibition of androgenic function. Cyto- and karyometric studies revealed a significant decrease in the area of the sperm head (8.24±0.24 mm2) and its nucleus (4.69±0.07 mm2), a decrease in the integral optical density of the sperm head ($p<0.001$), which indicates a decrease in the DNA content in the nucleus [23].

The effect of genital infection in men on the physiology of reproductive processes can be explained as follows:

1) direct and indirect effect of the infectious agent on sperm;
2) violation of the secretion of the genital glands has an indirect effect on the functional state of sperm;
3) inflammation and subsequent sclerosis in the tissues where sperm are formed or moved;
4) immunological reactions that depress fertility [24].

Recently, much attention has been paid to the autoimmune mechanism of infertility development in acute epididymitis. The decisive factor in this case is the spread of the inflammatory process to the testicle and the violation of the integrity of the hematotesticular barrier, the morphological substrate of which is a set of structures located between the lumen of the capillaries and the lumen of the seminal tubules. Violation of the integrity of this barrier opens the access of immunocompetent cells to the autoantigens of developing spermatogenic cells, which leads to sensitization and the production of antisperm antibodies, followed by the transfer of the autoimmune process to the contralateral organ and the development of autoimmune orchitis [23].

MODERN APPROACHES TO THE TREATMENT OF ACUTE EPIDIDYMITIS.

The basis for the treatment of acute epididymitis and epididymoorchitis is antibacterial therapy. The choice of an antibacterial drug for the treatment of inflammatory processes in the organs of the scrotum depends on the degree of its penetration into the parenchyma of the testicle and appendage, as well as on empirical ideas about the causal microorganism that caused the disease in each case.

The European Association of Urologists recommends fluoroquinolones as the drugs of choice for the treatment of acute epididymitis. At the same time, it is proposed to give preference to fluoroquinolones acting on C. trachomatis (for example, ofloxacin, levofloxacin), due to their wide range of activity and good penetration into the tissues of the genitourinary system. If C. trachomatis is detected as the causative agent, therapy should also be continued with doxycycline at a dose of 200 mg / day, while the total duration of treatment should be at least 2 weeks. Macrolides can be used as alternative drugs (degree of recommendations C) [20].

Studies by Razina S. E. (2010) also indicate the expediency of using modern fluoroquinolones - ofloxacin and levofloxacin, whose clinical efficacy in the treatment of patients with acute epididymitis is 90%; microbiological - 88.0% and 90.6%, respectively. At the same time, it was shown that in conditions of acute inflammation of the epididymis, the bioavailability of these drugs increases - for ofloxacin by 1.25, and for levofloxacin by 1.32 times [21].

Along with antibacterial therapy, a complex of other therapeutic effects is used. It is mandatory to give the scrotum an elevated fixed position, compliance with bed rest. Many authors speak about the expediency of local application of cold (cold compresses, ice), which reduces the severity of the local inflammatory reaction.

The not always satisfactory results of treatment of acute epididymitis with antibacterial therapy, in the form of frequent transition of the disease into a chronic form, the formation of long-term non-absorbable infiltrates and the development of scar-adhesive changes that subsequently lead to impaired fertility, prompted a number of authors to propose and investigate additional methods aimed at improving the results of conservative therapy [24].

According to a number of authors, improvement in the results of treatment of acute epididymitis can be achieved by including laser-magnetic effects on the scrotum in the therapy, which reduces the duration of the acute phase of inflammation by more than 2 times, increases the resistance of testicular tissues to secondary alteration and corrects endocrine and immune status disorders.

Currently, the possibility of using photodynamic therapy in the complex treatment of epididymoorchitis is being actively studied at the Bukhara State Medical Institute. Studies have shown that this technique makes it twice as effective to stop acute inflammatory changes, which in turn reduces the duration of stay of patients in the hospital and leads to an acceleration of their social rehabilitation [25].

Indications for surgical treatment in the development of acute epididymitis and its volume are still the subject of discussion.

There is a point of view according to which all patients with acute epididymitis are subject to surgical treatment, regardless of age, etiology and severity of the disease. Proponents of this approach claim that operational tactics allows timely diagnosis of ischemic lesions of the scrotum (testicular torsion or Morgania hydatides), and also makes it possible to stop the inflammatory process faster and reduce the length of stay of patients in the hospital by 2-3 times [27]. The authors' study of the long-term results of treatment of patients with acute epididymitis in the period from 2 to 4 years showed the best indicators of spermogram and erectile function in patients undergoing surgical treatment compared with patients receiving conservative therapy [27].

Arbuliev M. G. et al. (2008), based on their own research, consider it appropriate to conduct early surgical treatment only in severe form of the disease (according to the classification of Fedorchenko). At the same time, a total inflammatory-purulent process in the appendage is an indication for epididymectomy, limited - for resection of the appendage, and testicular necrosis or purulent melting of it - for orchectomy. In the absence of obvious signs of destruction in the severe form of the disease, the authors recommend using the notching method developed by them, which consists in applying multiple incisions up to 5 mm to the appendage and the protein shell. It is assumed that ultrasound and visual inspection do not allow to identify small abscesses, which are subsequently detected during histological examination, while the application of incisions allows you to open microabcesses and decompress the organ, which favorably affects the course of the disease.

The need for early minimally invasive interventions (incision) at the first signs of the transition of the process to the purulent-destructive stage is confirmed in the studies of D. V. Koryukov (2010), while the author recommends MRI to identify foci of destruction [31].

Summing up the above, it can be stated that conservative and wait-and-see tactics have become the most widespread in the treatment of acute epididymitis to date. It implies conservative therapy and the use of surgical intervention only with the development of purulent complications. At the same time, the not always satisfactory results of conservative therapy and the high frequency of reproductive function disorders after acute epididymitis have led to the development of numerous methods aimed at improving the results of conservative therapy and surgical treatment. In our opinion, the use of photodynamic therapy in conservative treatment and also operative treatment for wound healing is promising in this direction [32].

Theoretical and clinical applications of PDT in the complex treatment of acute epididymitis.

To achieve the research goal and solve the tasks set, general clinical, laboratory, ultrasound studies, immunological parameters of blood plasma, bacteriological methods of urine and pathological material examination, methods of statistical analysis will be used. Intraoperative and postoperative photodynamic therapy with 0.05% methylene blue solution with a red light source LED lamp of domestic production "VOSTOK -010203" was applied [21].

Most researchers associate the PDT effect with to denote the effect of light exposure on biological tissue, which increases significantly with increasing oxygen pressure in tissues. It is generally recognized that bacteria do not have a mechanism of protection against free radicals, but the degree of susceptibility to their increase varies from death - for anaerobes (bactericidal effect), to growth retardation for aerobes (bacteriostatic effect).

Strengthening of the mechanisms of nonspecific protection is an indirect effect on the bactericidal capabilities of granulocytes and macrophages by increasing or restoring normal oxygen pressure in the affected organs [25, 29].

Immunomodulatory effect - A number of studies have shown the immunostimulating effect of PDT. This effect is noted by Gramenitsky A. B. et al. (1996), based on the experience of using PDT (9-10 sessions) in 101 patients with sepsis and 10 healthy individuals. According to the authors, PDT increases the number of T cells in peripheral blood and normalizes the level of B lymphocytes. PDT also contributes to the normalization of lymphocyte differentiation processes and the involvement of mature T and B lymphocytes in the immune process, changes the functional activity of immunocompetent cells, activates cell-mediated immunity: the index of lymphocyte migration decreases when PHA is stimulated, the activity of humoral immunity factors increases [14].

Increased activity of antibacterial drugs in the focus of inflammation - the activity of antibacterial drugs such as aminoglycosides, some sulfonamides, fluoroquinolones, vancomycin and trimethoprim is reduced in hypoxia and is restored with an increase in oxygen pressure in ischemic tissues [22].

Photodynamic therapy in patients with acute epididymitis is being studied (2023), where PDT was used on the 1st day after surgery (dissection of testicular membranes and their drainage) in 15 patients with acute epididymitis and 6 patients with epididymoorchitis. The course of treatment included 5-6 sessions, lasting 15 minutes as a result of the treatment after surgery, accelerated wound healing was observed, which indicates the high efficiency of PDT and allows it to be recommended for widespread introduction into clinical practice [31].

CONCLUSION. The analysis of literature sources shows that acute epididymitis is a complex problem, both social and medical. This is determined by its high prevalence among men of reproductive age, the negative effect of the inflammatory process in the appendage of the testicle on reproductive function, as well as the possibility of severe complications that can lead to organ-bearing operations and death. Dissatisfaction with the results of traditional methods of treatment dictates the need to search for new types of effects on the inflammatory process in the testicle and its appendage.

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