STUDY OF IMMUNOSUPPRESSIVE PROCESSES AFTER KIDNEY TRANSPLANTATION

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Abstract: Kidney transplantation is the treatment of choice in patients with end-stage chronic renal failure (CRF). All over the world, there is a constant increase in the number of such patients. More than 370,000 patients receive renal replacement therapy in the United States. In 2002, more than 11 thousand kidney transplants were performed in the countries of the European Union, and in the USA - more than 12 thousand kidney transplants.

Keywords: organ transplant, acute rejection, immunological tolerance, chronic renal failure.

Even more urgent is the problem of treating end-stage chronic renal failure for our country, where the provision of patients with end-stage chronic renal failure with renal replacement therapy is insufficient. More than 10,800 patients are currently receiving treatment with hemodialysis and peritoneal dialysis in Russia, more than 2,500 patients with a functioning renal transplant are observed, however, the real need for renal replacement therapy is much higher (5). Kidney transplantation makes it possible not only to achieve a high quality of life for patients with end-stage chronic renal failure, but also to provide specialized care to a large number of patients in conditions of a shortage of dialysis sites.

However, a number of important problems still remain in clinical transplantation, one of which is the problem of infectious complications after kidney transplantation.

It was found that during the first year after LT, among all fatal complications, infections are the most significant, the proportion of which is at least 1/3 (1). Subsequently, infectious complications recede into second place after cardiovascular complications, but they continue to remain the most important cause of morbidity and mortality in patients with kidney transplants. The development of infectious complications after transplantation depends on the immunological status and the epidemiological environment. Immunological status is determined by the type of immunosuppressive therapy used, doses and sequence of drugs used, and the duration of treatment. An important influence is also exerted by the presence of uremia, neutropenia, anemia, hypoprotsinemia, hyperglycemia, and damage to the skin (4). Infections are not only one of the most frequent complications of the post-transplant period, but are often characterized by a severe course, unusual symptoms, which complicates the diagnosis and choice of treatment tactics. Unfortunately, so far there

are no immunosuppressive drugs that are absolutely free from infectious complications. The search continues for the most effective and at the same time safe regimens of immunosuppression after kidney transplantation (3). However, the incidence of infections with new immunosuppressive protocols is not fully understood. For example, there is still insufficient data on the frequency and nature of infectious complications when a new and already widely used drug mycophenolate mycophenolate mofetil (cellsept) is included in the immunosuppression protocol.

Of particular importance after organ transplantation are viral infections, most often caused by herpes viruses, primarily cygomegalovirus, Herpes simplex (type 1, 2), Herpes zoster, Epstein Barr viruses, as well as hepatitis B, C, D viruses (7). It has been established that viruses are the cause of at least 50% of all infectious complications in renal transplant recipients. The clinical significance of these infections is determined not only by the primary damage to organs and systems, but also by their immunomodulatory effect, which creates the preconditions for the development of severe superinfections, including aspergillosis, pneumocystosis, and mycoplasmosis.

A special place in clinical transplantation is occupied by cytomegalovirus infection (CMV infection), the causative agent of which is a virus from the beta-herpesvirus family. This is due to the high incidence of active CMV infection in the post-transplant period - from 20 to 60% in various transplant centers and a serious prognosis if specific therapy is not prescribed on time (2).

Treatment of patients with wound, pulmonary and urinary infections after kidney transplantation often becomes a difficult task due to the constantly changing sensitivity to antibiotics of pathogens of bacterial infections with a tendency to develop drug resistance, immunosuppressive status of patients (3). It is necessary to search for new strategies for the treatment and prevention of bacterial complications. There is no information in the available literature on the use of such a promising approach to the treatment of infectious-purulent complications as the use of bacteriophages in transplantation. At the same time, interest in phage therapy has revived in general surgical practice, oncology, and pediatrics (Perepanova T.S. et al., 1995; Lakhno V.M., Bordunovsky V.N., 2001).

One of the most challenging tasks for transplantologists and nephrologists is the management of renal transplant recipients with fever of unknown origin. The list of possible causes of this condition is very large, and the clinical picture does not have characteristic features that allow a nosological diagnosis to be established without the use of complex laboratory methods of examination. Creation of an algorithm for examination and treatment of renal transplant recipients with fever of unknown origin can shorten the diagnosis time and improve the quality of treatment for this group of patients.

One of the greatest achievements of the twentieth century is organ transplantation, which has stepped into medicine as a therapeutic alternative for organ failure and allows many patients to be saved from death for whom other options for survival do not exist. [17,24] Over 106,000 organ transplants were performed worldwide in 2010, and this is an indicator of the level of development of medicine in the state. Over the past three decades, the one-year survival rate of transplanted organs has reached 90% (kidneys, liver), but the duration of their functioning due to the development of chronic transplant rejection has changed insignificantly. Acute rejection even after liver transplantation was noted in 1/3 of patients. In most cases, it is dealt with using only traditional therapy, but in case of treatment-resistant rejection or contraindications to such treatment, it is necessary to use other means [19,21]. Prevention and therapy of acute rejection are effective, but are associated with significant risks, including opportunistic infections, recipient intoxication, metabolic disorders, and malignant neoplasms. The development of new therapies that do not compromise the immune system, but specifically prevent damage to allogeneic tissues, is of paramount importance for the future of transplant medicine. Induction of immunological tolerance will eliminate the need to take medications without rejection and associated side effects [12].

To achieve a state of tolerance, researchers have focused on studying the regulation of the immune response as the cornerstone of modern clinical transplantation. Observations in veterinary medicine of induced hematopoietic chimeras [3] and the pioneering work of M. Hasek and V. Demikhov, carried out back in the 50s. XX century, allowed to come closer to understanding this issue [14, 15].

The immunological nature of graft rejection was demonstrated by Peter Medawar in an experiment on the transplantation of a genetically alien skin graft in rabbits [8]. Both humoral and cellular mechanisms play a role in transplant rejection. Cellular rejection mechanisms cause T-lymphocytes to become sensitized to the transplanted antigens. [11,22] These lymphocytes cause damage to cells of foreign tissue by either direct cytotoxicity or secretion of lymphokines. T cell damage is characterized by parenchymal cell necrosis, lymphocytic infiltration, and fibrosis. Humoral mechanisms are mediated by antibodies that may be present in the serum of the recipient before transplantation or develop after transplantation of foreign tissue. Humoral factors damage the transplanted tissue through reactions that are equivalent to type II and III hypersensitivity reactions. The interaction of antibodies with the antigen on the surface of the transplanted cells leads to cell necrosis, and the accumulation of immune complexes in the blood vessels activates complement, which leads to the development of acute necrotizing vasculitis or chronic fibrosis of the intima with vasoconstriction.

Conclusion. Renal transplantation, renal transplant complications, impaired adaptation of the donor organism to the transplanted kidney are associated with the

immunogenesis of the individual organism. Changes in the physiological activity of class T lymphocytes in the body after kidney transplantation are accompanied by changes in all immunogenetic conditions in the body, which leads to a decrease in renal vital signs, resulting in renal complications, decreased vital signs of renal transplantation within three years.

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