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Case Report

Autoimmune Features of the Development of Renal Amyloidosis in Children

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Abstract

In this article, the authors reviewed the literature, as a result, it was revealed that the pathogenesis of autoimmune diathesis, rheumatoid arthritis and rheumatoid nephritis in children has a general immunopathological nature. However, autoimmune diathesis is an important risk factor for the onset and progression of rheumatoid arthritis and the subsequent development of renal amyloidosis based on immunopathological reactions in these patients.

Keywords: Nephropathy; Autoimmune Diathesis; Rheumatoid Arthritis

Introduction

Currently, rheumatoid arthritis (RA) has become medical and social problem, etc., attracts serious attention rheumatologists and pediatricians, which is due to a noticeable increase in cases diseases among children, often with a severe and progressive course diseases with a tendency to early disability of patients. According to WHO 1/10 of incapacity for work and 1/3 of disability accounted for by rheumatic diseases [1,46]. In recent years, some progress has been made in diagnostics and therapy for RA. Despite this, many aspects of this problem remain unclear. studied. So, a lot of work remains to be done to determine the main risk factors, pathogenesis, clinical features of RA in children, finding out the reason for the chronicity of the inflammatory process, improvement of diagnostic criteria and treatment methods, which has great importance for the prevention of early disability among population. Renal damage at the onset of RA is prognostic an unfavorable sign indicating a high degree activity and severity of the course, high risk of poor outcome of the disease, which often proceeds latently, has a tendency to progress and its result is a secondary contracted kidney with the development of chronic renal failure and death of the patient from uremia. Currently, the definition of clinical and laboratory markers, typical for different types of RA in comorbidity with different pathologies, including autoimmune diathesis (A and D) and early prevention of complications remains a priority area of scientific research.

The Republic of Uzbekistan pays special attention to health protection mother and child, to improve efficiency, quality and availability health care, support for a healthy lifestyle and prevention diseases, including through the formation of a system of medical standardization, introduction of high-tech diagnostic methods, treatment and effective models of clinical examination [29,32]. In this plan improving the health of children, especially in early childhood, improving diagnosis, treatment and early prevention of complications of autoimmune diseases in the most modern ways is important in medical practice.

Modern understanding of autoimmune diathesis in children

The constitution is a set of relatively stable morphological and functional properties of a person, due to heredity, age, as well as long-term and intense environmental influences, which determines the functional ability and the reactivity of the organism [5,14,16]. Diathesis is a genetically determined feature of the body, determining the originality of his adaptive reactions and predisposing to 3 a certain group of diseases, i.e., "Hereditary predisposition". The risk factors for the formation of many diseases are not only in the influence of the environment, but sometimes, to a greater extent, in constitutional characteristics of the body. It is believed that the majority chronic diseases is based on the constitution of the sick. In that sense of diathesis is considered as a pre-disease. Isolation of this or that type of diathesis helps in the development of recommendations for primary prevention of possible future diseases [30,31]. Thus, diathesis is a predisposition, pre-illness, pre-insufficiency of certain metabolic mechanisms. Define predisposition and degree of risk of the disease much more difficult than making a diagnosis of an already developed disease, even in cases of its minimal manifestations Predisposition (or diathesis) to diseases is determined by the characteristics of the structure and function one or several body systems: immune, central nervous system, neuro-humoral [10-12,35].

The amplitude of fluctuations in the "normal" functioning of the body very individual. Extreme indicators of the norm and compensated metabolic defects are the essence of predisposition (diathesis). In cases where the body cannot provide adaptation to changing environmental conditions, the predisposition is realized by the disease. IN currently, there are about 20 types of diathesis, combined into groups: I. Immunopathological: atopic, autoimmune, lymphatic, infectious and allergic. II. Dysmetabolic: uric acid, oxalate, diabetic, hemorrhagic, adiposodiathesis. III. Organotopic: nephrotic, intestinal, hypertensive, cardioischemic, atherosclerotic. IV. Neurotopic: psycho-asthenic, vegetative-dystonic [11,13,14,16,25,43].

The basis of autoallergic diathesis is the inability to the formation or maintenance of immunological tolerance for four in relation to their own antibodies (own cells, proteins or nucleic acids) under the influence of various, most often infectious stimuli (cytomegalovirus) [39]. Distinguish between organospecific form (lupoid diathesis), causing a predisposition to the occurrence in children of systemic lupus erythematosus, rheumatoid arthritis, some connective tissue diseases, immunohemopathies, and organ-specific, underlying the formation of organ pathology such as autoimmune thyroiditis, orchitis, encephalitis, etc. [31].

Autoimmune diathesis

(autoimmune reactions, "lupoid diathesis ") hypersensitivity of the skin to ultraviolet irradiation, a significant increase in the level of gamma globulins in the blood, often identification of LE cells, antinuclear factors, in a state of complete clinical well-being, polyclonal activation of B-lymphocytes, and also T-helpers with a decrease in the activity of T-suppressors, increased, spontaneous blast transformation of lymphocytes or its activation by tissue antigens, elevated IgM levels, hypocomplementemia (especially deficiency of C3 complement [16,38,46]. According to American authors, congenital tendency to autoimmune diseases is traced in 10% of the US population, penetrance among women is 2 times higher than among men [33,36]. Study the role of persistent viral infections inprovoking the transformation of diathesis into an autoimmune disease.

Prevention of diseases to which children with diathesis, should begin before the birth of the child [19]. Even before pregnancy, it is necessary to take care of the treatment of chronic genital and extragenital pathology in the expectant mother. Pregnant woman must follow a rational diet. Elimination is essential from the first 7 months of pregnancy, occupational hazards, excessive sun exposure, cessation of active and passive smoking, adverse effects of various radiation, medicines. Should keep in mind that prolonged breastfeeding is an important factor in the prevention of many diseases. Questions and Answers nutrition of children with diathesis are key to prevent the development of diseases such as atopic dermatitis, bronchial asthma, food allergies. Nutrition also plays an important role in preventing development of metabolic diseases [9-11,19].

An essential point in preventing the development of diseases environmental control It is known that frequent infectious diseases, allergic diseases are directly related to unfavorable conditions in the environment [10,11]. Strengthening the immunological reactivity of the body of such children by hardening, organization of a rational lifestyle, the use of adapagens, immunomodulators will help reduce the incidence of infectious diseases and pathological conditions to which children with diathesis [21,25]. Data from

sources suggests that children with autoimmune diathesis have a higher risk of developing various autoimmune diseases in the future. From a pathogenetic point of view, comorbid the course of autoimmune diseases, including rheumatoid arthritis with autoimmune diathesis, accelerates the development of visceral changes (nephropathy) [41,42]. New views on immunopathological processes in rheumatoid arthritis in children Rheumatoid arthritis (RA) in both adults and children is is a common disease from the group of collagenoses, which is based on immunological processes and characterized by cyclic prolonged or a chronic course with systemic damage to the connective tissue, mainly of the musculoskeletal system [1-3,8]. The social significance of this disease is extremely high, because it tends to become more widespread throughout the world, leads to early disability and disability of patients [33,46].

RA is registered in all countries of the world with different climatic and geographical conditions with a frequency of 0.6 to 1.5% [1,18,20,24]. Moreover, the disease develops more often in women than in men. By data from sources in various climatic and geographical zones of the CIS RA suffer from 0.24 to 1.5% of the adult population, and abroad - from 1 to 3.3% population. A particularly high incidence of RA was found among relatives. First degree of relationship (3.5%), and the highest incidence rate (5.1%) found in women of the first degree of relationship. In families of patients RA is much more common than in the general population, rheumatic fever and other autoimmune and infectious-allergic diseases, i.e., family aggregation is observed, which may be due to a hereditary predisposition to influences environmental factors (past infectious diseases, physical and psychological trauma, hypothermia, etc.). According to epidemiological studies, the incidence of RA among children in the USA it was up to 10 cases, in Europe - 5-10 cases, in Finland - 19.6, in England - 16-27 cases per 10,000 child population [37,38]. Among the child population in Uzbekistan, the RA ranges from 0.08% to 2.1% cases [1].

In children with RA, in about half of cases, it begins before the age of 5-7 age, much less often before the first year of life and after 13 years. Wherein, girls get sick 1.5-2 times more often than boys [1,38]. Increased degree of age risk, predominant spread of the disease in girls, apparently associated with early physiological hormonal abnormalities of the body. The factors contributing to the onset of RA are numerous. A number of authors point to the etiological role of streptococci, staphylococci, diphtheroids, clostridia, chlamydia, yersineous infections, mycoplasmas, rickettsiae as possible causative agents of RA. Other researchers believe that RA is caused by parvoviruses, hepatitis B viruses, rubella viruses. Many authors cite information that the causative agents of the disease are Epstein-Barr viruses, localized in B-lymphocytes and having the ability disrupt the synthesis of immunolobulins [44].

However, to date, no convincing data have been received indicating the specificity of any particular of of the above microorganisms as the causative agent of RA. In some cases, a factor that provokes the development of RA in children, there may be joint injury. Some researchers dismiss the decisive the role of food agents and unfavorable social and living conditions in the occurrence of RA. A number of authors believe that in the development of the RA a large importance belongs to endogenous factors - age, genetic and endocrine [38]. According to these researchers, various adverse environmental influences (intercurrent diseases, hyperinsolation, physical trauma, psychological factors, the use of some medicines, etc.) activate the initial infectious agent, which is a trigger in the development of immune response reactions in the body, predisposed to the development of pathological process.

Currently, the vast majority of researchers recognize the great role of hereditary predisposition in development RA in children. Research by scientists has shown that the likelihood of the risk of development diseases in children in families where there are patients with any collagen diseases increases by 4.7 times. In the research of S.A. Rakhimov [20] also emphasizes the importance and great role of the family factor in the occurrence of RA in children. The development of this pathological process is associated not so much with features of the primary agent, how much with an individual reaction organism on its impact. This reaction is largely genetically determined. Therefore, in recent years, when learning the role of hereditary mechanisms in the pathogenesis of RA is attention to the study of antigens of the main histocompatibility complex. Quite a number of studies point to the presence of an associative relationship of HLA antigens with clinical signs diseases, which indicates their predictive value in relation to the nature of the course and outcome of the disease [38]. It is noteworthy that a number of researchers found the presence of the same antigenic associations of the HLA complex in children and adults suffering from RA, this confirms the unity pathogenetic mechanisms in this

disease in children and adults, since there is no such form of RA in adults that would not occur in children; the difference lies only in the frequency of specific clinical forms diseases in adults and children. Therefore, it is reasonable to view a number of authors on RA as a heterogeneous disease in adults and children Currently, the overwhelming majority of researchers believe that the pathogenesis of RA is based on an immunoregulation disorder various etiological factors on the body, which is different genetic predisposition to the development of the disease [1-3].

Modern features of kidney damage in rheumatoid arthritis in children

In the overwhelming majority of cases, the pathological process with RA is localized at the beginning of the synovial membrane of the joints, but in further changes in the connective tissue of other organs are observed. At the heart of the defeat of many organs and systems are vasculitis, which immunocomplex character [1-3,8,34,37]. The severity of clinical and laboratory manifestations of damage to other organs and systems in RA depends on the clinical form of the disease. In patients, predominantly the articular form of the disease in the clinical picture appears at the first plan to damage the joints, while manifestations of damage to other organs absent or very weakly expressed, and with articular-visceral form, along with articular syndrome, already at the onset of the disease there are clear signs of damage to various organs and systems [5,15].

Lymph node involvement may occur in patients with RA (lymphadenopathy), nervous system, spleen and gastrointestinal tract (amyloidosis, gastritis, enteritis, colitis), liver (hepatitis, dystrophy, necrosis, cell sclerosis), muscular system (degeneration, atrophy), lungs (interstitial pneumonia, pneumosclerosis), heart (carditis), major endocrine glands - pituitary gland, thyroid gland, adrenal glands, pancreas and eyes [24,28]. The defeat of these organs and systems contributes to a more severe course of the disease, creates additional difficulties in treating patients and aggravates the prognosis pathological process [8,21].

In recent years, the attention of researchers has attracted more functional state of the kidneys in RA. It has been established that the kidneys are the disease is affected in about 50-60% of cases and their involvement in the pathological process can manifest itself in the form of amyloidosis [26,33], glomerulonephritis, nephroangiosclerosis, interstitial nephritis and eleven pyelonephritis [4,36]. It was found that nephropathy in patients RA often presents with varying degrees of proteinuria, microhematuria and leukocyturia, signs of renal failure, but often clinical signs were absent, which was the basis to the allocation of the subclinical stage of the renal process in patients with RA. Later studies using immunohistochemical and electron microscopic methods made it possible to detect in patients RA is practically all morphological types of glomerulonephritis. Clinical and laboratory symptoms of kidney damage in RA can be manifested by swelling of the face, scrotum, legs and feet or only proteinuria of varying severity or hematuria, arterial hypertension, nephrotic syndrome or and isolated urinary syndrome. Kidney damage in RA can be prolonged time to pass latently, or to progress steadily and rapidly, the result of which is a secondary contracted kidney with a clinical picture chronic renal failure [9].

A number of authors suggest that the occurrence of glomerulonephritis in RA is a pre-stage of renal amyloidosis [24,37]. According to H.L. F. Currey and J. Woodlend Prescribing Prednisolone in Patients with RA lesions kidneys led to an improvement in the condition of patients and the elimination of clinical and laboratory manifestations of glomerulonephritis. However, many scientists do not found positive dynamics of the renal process in RA patients when prescribing corticosteroid drugs, and according to some authors use of anti-inflammatory drugs and corticosteroids can even lead to an increase in clinical and morphological symptoms of kidney damage in this disease [38]. Some authors, based on the results of their own studies also concluded that the appointment of nonsteroidal anti-inflammatory drugs can in some cases aggravate kidney damage in RA [40]. In addition, the literature provides 12 messages, the authors of which link the occurrence of nephropathy in patients with RA with the appointment of gold preparations, D-penicillamine, cyclosporin A, levamisole. However, most researchers consider kidney damage in this disease ai pathognomonic sign, which is one of the manifestations immunocomplex pathology [20].

The incidence of AA-amyloidosis of the kidneys in RA in children is from 0.8 to 2.0%, in adults with RA duration of 28.3 years - 8.9% [3,46]. IN In recent years, against the background of immunobiological therapy, the frequency of AA-amyloidosis of the kidneys in adults has decreased to 2.5% [37]. On the to date, the main mechanism of development of AA amyloidosis has been es-

tablished, which consists in a constant or periodic increase serum amyloid A (SAA) concentration. It was found that the synthesis SAA is influenced by pro-inflammatory cytokines: IL-1, IL-2, IL-11, IL-6, TNF-α and others. To realize the amyloidogenic potential of SAA, it is necessary not only the effect of the inflammatory process in the body, but also its duration.

The role of genetic factors in the development of AA-amyloidosis of the kidneys in RA. AA-renal amyloidosis most often develops in children with a systemic form, in adults - with systemic and polyarticular forms of RA. The first symptom of AA renal amyloidosis is isolated proteinuria, which transforms into nephrotic syndrome [22,23,47]. Features of the nephrotic syndrome are in the absence in most cases hypercholesterolemia, combined in some patients with arterial hypertension, hematuria, impaired renal function [45]. The main method for confirming the diagnosis of AA-renal amyloidosis, is an intravital morphological study of the kidneys. Enhancement blood SAA level in children with RA reflects the degree of the inflammatory process and is considered as a risk factor for the development of AA-amyloidosis of the kidneys [6,9,17,18]. In this case, the use of immunobiological drugs (tocilizumab, anakinra) has therapeutic efficacy [7,48].

Along with joint damage in patients with RA, involvement in pathological process of other organs and systems [17]. One of pathognomonic visceral signs of the process, a number of authors consider kidney damage, which can manifest itself as an overt clinical picture, but more often it proceeds latently and is diagnosed only when application of special research methods [39]. Kidney involvement in the pathological process is an unfavorable prognostic sign, since the result of kidney damage in these patients may be development of chronic renal failure [26-29].

Summarizing the above data of the special literature, one can conclude that damage to joints and other organs in RA is a consequence of the development of immunopathological reactions in individuals genetically predisposed to the onset of this disease. Immune the nature of RA is confirmed by the identification of rheumatoid factor in patients, various autoantibodies, immune complexes sensitized to components of the connective tissue of lymphocytes, the similarity of focal pathological changes with the manifestation of immune inflammation, impossibility of detecting an infectious agent and ineffectiveness anti-infectious therapy with the effectiveness of treatment of patients immunosuppressive drugs [45].

Conclusion

However, literature data on the pathogenesis and nature of clinical and laboratory manifestations of renal disorders in this disease in adults are few in number and contradictory, while the renal pathology in children with RA remains generally poorly understood problem and until now there have been no comprehensive studies in the comorbid course of RA in children with immunodeficiency pathologies, including AID, which remains relevant in pediatric and adult rheumatology. Fourteen Thus, the presented data indicate that pathogenesis of autoimmune diathesis, rheumatoid arthritis and rheumatoid nephritis in children has a general immunopathological nature. But autoimmune diathesis is an important risk factor for the occurrence and progression of rheumatoid arthritis and subsequent development amyloidosis of the kidneys based on immunopathological reactions in such patients.

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