Volume 2, Issue 6, June 2024 ISSN (E): 2938-3765

NEW VIEWS ON THE PATHOGENETIC MECHANISMS OF CHRONIC GLOMERULONEPHRITIS

Umarova Tamila Abdufattoevna
Assistant of the Department of Clinical Laboratory
Diagnostics with a Course of Clinical and Laboratory Diagnostics PGD;

Kudratova Zebo Erkinovna
PhD, Associate Professor of the Department of Clinical Laboratory
Diagnostics with a Course of Clinical and Laboratory Diagnostics PGD;

Kosimova Sabina
Cadet (Laboratory Doctor) of the Department of Clinical Laboratory
Diagnostics with a Course of Clinical and Laboratory Diagnostics PGD;

Nafasova Zarina
Cadet (Laboratory Doctor) of the Department of Clinical Laboratory
Diagnostics with a Course of Clinical and Laboratory Diagnostics PGD;
Samarkand State Medical University Samarkand, Uzbekistan

Abstract
Chronic glomerulonephritis (chronic nephritic syndrome) is a group of diseases heterogeneous in origin and pathomorphology, characterized by immunoinflammatory damage of the tubules, tubules and interstitium of both kidneys and progressive course, resulting in the development of nephrosclerosis and chronic renal failure.

Keywords: chronic glomerulnefritis, genetic predisposition, leukotrienes, cytokines, neutrophils.

Introduction

Chronic glomerulonephritis can be a consequence of acute glomerulonephritis. Along with this, primary chronic glomerulonephritis without a previous acute period develops. The main etiologic factors of chronic glomerulonephritis are similar to those of acute glomerulonephritis. Very often the cause of the disease cannot be clarified. The role of genetic predisposition to the development of chronic glomerulonephritis is also widely discussed [1,3,5].

The mechanism of development of chronic glomerulonephritis is generally similar to the pathogenesis of acute glomerulonephritis, i.e. it is also based on immune inflammatory process, the development of which involves the deposition of antibodies and complement fragments, the formation of complement-membrane damaging complex, blood coagulation factors, leukotrienes, cytokines, neutrophils, platelets, macrophages, T-lymphocytes [2,4,6].

The main pathogenetic variants of chronic glomerulonephritis are similar to those of acute glomerulonephritis. However, there are certain features of pathogenesis of some morphologic

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

Licensed under a Creative Commons Attribution 4.0 International License.

variants. A number of authors also emphasize the major role of genetic inferiority of T-cell immunity in the development of chronic glomerulonephritis. Studies of a number of nephrology centers have allowed to formulate a hypothesis of the origin of chronic glomerulonephritis. According to it, due to genetic predisposition there is an insufficient supply of early lymphoid (trophic) elements to the kidney. This disrupts the normal physiological repair of individual parts of the nephron and promotes the formation of an inflammatory infiltrate in the kidneys with the participation of T-lymphocytes, mononuclear cells, the release of a large number of cytokines that increase the proliferation of glomerular cells, cause damage to all structures of the nephron, primarily 9 basal membrane, with the subsequent formation of immune complexes [7,8].

It is generally recognized that the development of chronic glomerulonephritis is based on immunopathologic processes. Both ongoing immune inflammatory reactions and non-immune mechanisms of progression are also involved in the progression of the disease: - development of progressive renal fibrosis; - hemodynamic factors; - metabolic mechanisms; - coagulation mechanisms; - tubulointerstitial sclerosis [8,10].

The immunoinflammatory process in the kidneys is accompanied by reparative changes, the outcomes of which are different: complete restoration of the structure of the tubules (usually under the influence of treatment or less often spontaneous) or in unfavorable course - the development of progressive fibrosis, which is the basis of chronic renal failure. Progressive renal fibrosis is caused by hyperfunctioning of glomerular cells and blood cells infiltrating renal tubules, which is accompanied by excessive accumulation of connective matrix and at the same time insufficient its utilization [11,12].

The leading role in the progression of glomerulosclerosis is played by mesangial cells. They have contractile, phagocytic and metabolic activity. As is known, mesangium is the connective tissue backbone of the tubules. Angiotensin II plays an important role in the development of progressive renal fibrosis. It not only causes intraclubular hypertension, but also stimulates proliferation of renal tubular mesangial cells, induces synthesis of transforming (platelet) growth factor - the main fibroblast growth factor - by smooth muscle and tubular cells [1,2,3].

Hemodynamic disorders (systemic and arterial hypertension) are the most important factors in the progression of chronic glomerulonephritis. Chronic progressive glomerulonephritis is characterized by loss of functioning renal mass, which leads to compensatory hypertrophy and hyperfunction of preserved renal tubules. Increase in their function is always accompanied by impaired intrarenal hemodynamics - intraclubular hypertension and hyperfiltration, which provides increased perfusion of the surviving nephrons [4,5,6].

Activation of the renin-angiotensin II system also plays a major role, which leads to spasm of efferent arterioles and increased pressure in the10 tubules. Increased pressure in the tubules promotes proliferation of mesangial cells and hyperproduction of mesangial matrix. The disturbed relationship between vasoconstrictive endothelial hormone - endothelin-1 - and vasodilating endothelial factor - nitric oxide - plays a major role in the disturbance of renal hemodynamics and progression of glomerulonephritis [7,8,9].

These substances are produced by the endothelium of renal vessels. In glomerulonephritis, endothelin-1 synthesis is activated, which is accompanied by renal vascular constriction, decreased renal blood flow, ischemic renal damage and, as described above, stimulation of fibrogenesis. The production of vasodilatory factor (nitric oxide) is decreased in chronic glomerulonephritis. The

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

Licensed under a Creative Commons Attribution 4.0 International License.

most important among metabolic disorders in the progression of chronic glomerulonephritis are lipid shifts [12].

They are most often observed in persons with nephrotic syndrome, but also develop in glomerulonephritis without this syndrome. Changes in lipid metabolism most often consist of an increase in blood cholesterol, triglycerides, low-density lipoproteins, unesterified fatty acids, an increase in the coefficient of atherogenicity. Dyslipidemia leads to deposition of lipids in the kidneys. Disorders of lipid metabolism are accompanied by nephrotoxic effect, and at deposition of lipids in renal structures there is simultaneously an increase in mesangial matrix, which indicates the fibrosogenic effect of lipid metabolism disorders [1,5,7,9].

Disorders of lipid metabolism in chronic nephritis are accompanied by activation of lipid peroxidation with the formation of free radicals and peroxide compounds that have a damaging effect on the kidneys and promote the development of fibrosis. The damaging effect of excessive calcium deposition in the kidneys has also been established, which is especially pronounced in chronic renal failure. Calcium accumulation in renal tissue contributes to the development of intraclubular arterial hypertension, mesangial proliferation, and fibrosis progression. It is now established that the most important mechanism of progression of chronic glomerulonephritis is local intravascular blood coagulation with the formation of microthrombi in the capillaries of the tubules and fibrin deposition in them [3,5,7].

Subendothelial fibrin deposits in the capillaries of the tubules are the most important criterion of unfavorable prognosis and progression of chronic glomerulonephritis. This is explained by the fact that fibrin deposits formed due to local hypercoagulation stimulate proliferation of endotheliocytes and mesangiocytes, formation of connective tissue in the kidneys, reduce microcirculation in the tubules, contribute to the development of ischemia in them. The leading role in the development of intravascular hemocoagulation in the kidneys is played by damage to the endothelium by immune complexes, cytokines, inflammatory mediators, various endotoxins, activated complement. At the same time there is platelet activation, increased adhesive-aggregation function and increased production of transforming growth factor. As a result of these processes platelet microaggregates are formed, coagulation link of hemostasis is activated, fibrin deposits are formed, synthesis of connective tissue is stimulated [11,12].

Tubulointerstitial sclerosis is now recognized as an important factor in the progression of chronic glomerulonephritis. The main role in the development of tubulointerstitial damage and sclerosis is played by renal tubule epithelial cells. They are activated and produce substances that promote renal interstitial damage and fibrosis. Activation of renal tubular epithelial cells is due to the production of cytokines by cells involved in inflammation, as well as protein reabsorption in the renal tubules. Persistent proteinuria has a toxic, damaging effect on the renal interstitium [8,9,10].

Thus, the above mechanisms of progression contribute to the development of a long-term inflammatory process that runs in a wave-like manner (with periods of exacerbations and remissions), which eventually leads to sclerosis, hyalinosis, desolation of the tubules, the development of chronic renal failure [2,3,4,9].

Diagnosis of chronic glomerulonephritis is based on the data of anamnesis, examination of the patient and a number of laboratory and instrumental studies.

The main methods of research include:

1. general blood analysis. A slight decrease in hemoglobin (Hb) concentration due to blood dilution is characteristic. COE is moderately elevated.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

Licensed under a Creative Commons Attribution 4.0 International License.

2. Biochemical blood analysis (determination of urea, creatinine, total protein, protein fractions, cholesterol and the entire lipid spectrum, sialic acids, fibrin, seromucoid). Biochemical manifestations of nephrotic syndrome are hypoproteinemia with hypoalbuminemia, dysproteinemia with predominance of α2- and less often γ-fractions of globulins, hyperlipidemia.
3. urine tests: - urinalysis: proteinuria, hematuria, leukocyturia (lymphocyturia). Relative density of urine is not reduced; - urine analysis according to Nechiporenko: micro- and macrohematuria, leukocyturia (lymphocyturia), erythrocytic cylinders; - urine analysis according to Zimnitsky: the state of renal concentration capacity (daily diuresis, the ratio of diuresis during the day and night, daily fluctuations in relative urine density); - determination of daily proteinuria - a quantitative method that takes into account daily diuresis and allows a more accurate assessment of the dynamics of proteinuria, including under the influence of treatment; - daily measurement of daily diuresis and the amount of fluid drunk [3,4].
4 Determination of antistreptococcal antibody titer (detection of antistreptolysin O (ASL-O), antistreptococcal hyaluronidase).
5. Reberg-Tareyev test (determination of the presence and degree of decrease in the rate of glomerular filtration and tubule reabsorption by endogenous creatinine).
Additional methods of research are:
1. Swab from the pharynx to detect streptococci.
2. examination of the ocular fundus. When BP increases, the following changes occur: narrowing of arterioles, sometimes the phenomenon of pathological arteriovenous crossing, edema of the optic nerve papilla, spot hemorrhages are possible.
3. Renal ultrasound. Kidney size is unchanged or slightly enlarged (normal length 75-120 mm, width 45-65 mm, thickness 35-50 mm). Swelling of renal tissue is detected. The calyx-lochanous system is unchanged.
4. BP monitoring. This is useful to detect arterial hypertension, especially not noticed by the patient, as well as to verify its severity (according to the study prescribe antihypertensive drugs and monitor the adequacy of therapy) [1,4,7].
Thus, the diagnosis of acute glomerulonephritis is based on the appearance of edema, headache, arterial hypertension, protein, erythrocytes and cylinders in the urine, changes in the biochemical analysis of blood in young people 10-14 days after angina or acute respiratory disease. An increase in blood titers of ASL-O confirms the streptococcal etiology of acute glomerulonephritis [2,5].

References

1. Kudratova Z. E. et al. Current modern etiology of anemia //Open Access Repository. – 2023. – Т. 10. – №. 10. – С. 1-4.
2. Burxanova D. S., Umarova T. A., Kudratova Z. E. Acute myocarditis linked to the administration of the COVID 19 vaccine //Центральноазиатский журнал образования и инноваций. – 2023. – Т. 2. – №. 11. – С. 23-26.
3. Кудратова З. Э. и др. Атипик микрофлора этиологияли ўткир обструктив бронхитларининг ў зига хос клиник кечиши //Research Focus. - 2022. - Т. 1. - №. 4. - С. 23-32.
4. Kudratova Z. E, Normurodov S. Etiological structure of acute obstructive bronchitis in children at the present stage - Thematics Journal of Microbiology, 2023. P.3-12.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

Licensed under a Creative Commons Attribution 4.0 International License.

5. Kudratova Z. E., Tuychiyeva S. K. Atipik mikroflora etiologiyali o'tkir obstruktiv bronxitlar etiopatogenezining zamonaviy jixatlari. Research Focus, 2023, B. 589-593.
6. Kudratova Z. E., Karimova L. A. Age-related features of the respiratory system. Research Focus,Tom 2, P. 586-588.
7. Исомадинова Л. К., Даминов Ф. А. Современная лабораторная диагностика хронического пиелонефрита у детей //Journal of new century innovations. – 2024. – Т. 49. – №. 2. – С. 112-116.
8. Isomadinova L. K., Daminov F. A. Glomerulonefrit kasalligida sitokinlar ahamiyati //Journal of new century innovations. – 2024. – Т. 49. – №. 2. – С. 117-120.
9. Isomadinova L. K., Qudratova Z. E., Shamsiddinova D. K. Samarqand viloyatida urotiliaz kasalligi klinik-kechishining o'ziga xos xususiyatlari //Центральноазиатский журнал образования и инноваций. – 2023. – Т. 2. – №. 10. – С. 51-53.
10. Isomadinova L. K., Qudratova Z. E., Sh B. F. Virusli gepatit b fonida Covid-19 ning klinik laborator kechish xususiyatlari //Journal of new century innovations. – 2023. – Т. 30. – №. 3. – С. 60-65.
11. Isomadinova L. K., Yulayeva I. A. Buyraklar kasalliklarning zamonaviy diagnostikasi //Центральноазиатский журнал образования и инноваций. – 2023. – Т. 2. – №. 10 Part 3. – С. 36-39
12. Kudratova Zebo Erkinovna, Tamila Abdufattoevna Umarova, & Sirojeddiova Sanobar. (2024). Modern types of immunoenzyme analysis methods old problems. Web of Discoveries: Journal of Analysis and Inventions, 2(6), 67–70.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

Licensed under a Creative Commons Attribution 4.0 International License.